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"To promote the study and dissemination of knowledge of the cause, prevention and control of diseases of the teeth, their supporting structures and adnexa and related subjects; and to foster and promote a better scientific understanding between the fields of dentistry and medicine."

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RECENT CONCEPTS ON CONNECTIVE TISSUE

GEORGE A. KRIKOS, D.D.S., Ph.D.*

The realization that the cells of the body are separated from the blood stream by connective tissue, through which nutrients from the blood and metabolic products of the cells must pass, emphasizes the importance of connective tissues in health and disease.

To the dentist, both the practitioner and the researcher, connective tissues are of great interest. Fibrous connective tisue, bone and cementum are varieties of connective tissue. Connective tissue and particularly epithelial-connective tissue interrelationships play a great role in tooth development and eruption. Inflammation, a basic pathologic process of great concern to the dentist, is intimately associated with connective tissue. Systemic disturbances, such as vitamin deficiencies, endocrine imbalances, etc., affect the oral connective tissues and thus alter their response to injury. The interrelationships between epithelial attachment and periodontal membrane are at the heart of the pathogenesis of the formation of the periodontal pocket. Finally, many treatments in dentistry aim at repair by connective tissue. The above facts make a review of the recent concepts on connective tissue most appropriate.

Connective tissue consists of an interlacing network of collagenous, reticular and elastic fibers lying in a non-fibrillar, amorphous matrix, the ground substance; scattered through the tissue are a variety of isolated cells. Consequently connective tissue consists of three main elements: cells, fibers, and ground substance. Neither the proportions in which these elements are mixed, nor their chemical composition is always the same. Such quantitative and qualitative differences give rise to the varieties of connective tissue such as fibrous connective tissue, bone, etc.

In this review, attention shall be directed particularly to the structural and chemical aspects of the intercellular substance of fibrous connective tissue and to the biosynthetic mechanisms involved in their formation.

COLLAGEN

STRUCTURAL AND CHEMICAL ASPECTS

General. Studies on the distribution of collagen in the animal kingdom[1] have shown that collagen is not an entity either from the chemical or from the large scale structural standpoint. We are not dealing with "collagen", but with the "family of collagens". Even among mammalian collagens there are differences. The differences become more marked as we move down the animal kingdom. In fishes, particularly cold water fishes, the hydroxyproline content and thermal shrinkage temperature are low as compared to mammalian collagen[2, 3]. The most marked differences reported are those seen in the so-called secreted collagens, such as the cuticle of the earthworm Lumbricus sp.[4, 5] Although these collagens give a high angle diffraction pattern similar to that of mammalian collagen, they show no axial periodicity. Recent studies have shown that the hydroxyproline content of earthworm cuticle is 50 per cent higher and its shrinkage temperature lower than that of mammalian collagen[6]. The studies on secreted collagens are of interest because they indicate that in certain cases collagen is of epithelial origin. The possibility, therefore, that the hydroxyproline[7] of enamel matrix may be an indication of the presence of a collagenous material deserves further investigation.

Physical properties. In large bundles, collagen is practically non-extensible and exhibits great tensile strength. When heated, collagen contracts, the temperature required varying with the source of the collagen.

* From the Department of Pathology and the Department of Dentistry and Dental Research, School of Medicine and Dentistry, University of Rochester, Rochester, N. Y. Present address: Assistant Professor of Pathology, School of Dentistry, University of Pennsylvania, Philadelphia 4, Pa.

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Chemical aspects. Collagen is a protein. Its amino acid composition, as determined by chromatographic methods, indicates that collagen is poor in aromatic amino acids and rich in nonpolar amino acids, glycine accounting for one third and proline and hydroxyproline for one fourth of the residues[8]. With the possible exception of elastin, collagen and its related substances are the only proteins known to contain hydroxyproline and hydroxylysine.

Even highly purified collagen appears to contain a carbohydrate moiety consisting of 0.4 per cent hexose in the form of glucose, galactose and mannose, and 0.05 per cent hexosamine[9].

Morphology. From the structural standpoint, collagen is a fiber from the level of observation of the light microscope down to that of the wide angle X-ray diffraction. At the microscopic level collagen appears as bundles of non-branching fibers having a constant diameter of 0.3 - 0.5 microns. These fibers in turn are bundles of fibrils with diameters of several Angstrom units; these are best examined with the electron microscope. The hypothetical thinnest unit of the fibril is the protofibril which is supposed to consist of an adlineation of collagen molecules. These are at present regarded as a coiled-coil system of three polypeptide chains.

When examined with the electronmicroscope collagen fibrils are seen to consist of alternating regions of greater and lesser density termed respectively bands and interbands. The period of this banding shows a distribution ranging from 400 A° to 1000 A°, with a maximum at 620-660 A°. The bands and interbands are believed to represent regions of relative disorder and order respectively caused by interaction between the side chains of adjacent collagen particles[10].

A similar wide-angle diffraction pattern is probably the only property that all collagens have in common. On the basis of the wide-angle diffraction data and other properties of collagen it is now generally agreed that it is possible to construct only two models, known as Collagen I and Collagen II, which are compatible with the data at present available. They represent a coiled-coil system of three polypeptide chains. The key to the design is the occurrence of glycine at every third position in the chains. The main difference between these two models is the way the backbones of the three chains are phased relative to one another[11].

THE BIOSYNTHESIS OF COLLAGEN AND THE FORMATION OF COLLAGEN FIBRILS

In a recent electronmicroscopic and chemical study of fowl embryo osteoblasts grown in tissue culture it was observed that the protein-or peptide-bound hydroxyproline content per milligram of dry weight tissue reached a maximum before the appearance of fibrils exhibiting a banding characteristic of collagen fibrils[12]. This observation strongly suggests that the appearance of banded fibrils is preceded by that of a hydroxyproline containing precursor which itself has no banded structure in the electronmicroscope. Most likely this precursor is not even a fibril.

The nature of the in vivo collagen fibril precursor. Studies dealing with the nature of this precursor are closely related to studies of the so-called soluble collagens. Today three collagen fractions are recognized: (a) neutral salt extractable collagen obtained by extraction of fresh connective tissues with cold, neutral or mildly alkaline salt solutions[13, 14] (b) acid citrate extractable collagen, known as procollagen, obtained by extraction of connective tissue with acid citrate buffer[15], and (c) insoluble collagen[16] which represents what remains after exhaustive extraction with neutral salt solution and acid citrate buffer.

The radioisotope studies of Harkness et al.[13] in rabbits using 14 C-labelled glycine as tracer, suggested that the neutral salt extractable collagen has the highest turnover rate and was almost certainly the *in vivo* precursor of all or most of the insoluble collagen, whereas the acid citrate extractable collagen was an intermediate for only part of the insoluble collagen. These suggestions recently confirmed by similar radioisotope[17] and chemical[17] studies on the carrageenin granuloma of the guinea pig, and by the observations of Gross[18, 19] that the neutral

salt extractable collagen content of the skin correlates closely and directly with the growth rate, are strongly in favor of the precursor role of this fraction.

There is evidence suggesting that neutral salt extractable collagen is not derived from the fibrils, but from extrafibrillar sources, such as the ground substance and/or the cells, where it may exist in a random molecular dispersion, small aggregate state, or in some non-random organization, which however, is different from the typical cross striated fibril[13, 20, 17]. If neutral salt extractable collagen is of extrafibrillar origin, morphologists must realize that the number of collagen fibers that can be distinguished histologically per unit area is not necessarily an index of collagen formation, but at best of collagen fiber formation.

In the light of the evidence already presented the contention of Orekhovitch[21, 22] that acid citrate extractable collagen is the *in vivo* precursor of the connective tissue fibril is not generally accepted. Radioisotope studies[23, 17] indicate that the acid citrate extractable collagen may be of fibrillar origin, derived from collagen recently laid down, this is from the outer layers of large fibers and from the thin argyrophilic fibers of developing or regenerating connective tissue. This hypothesis has been substantiated by electronmicroscopic studies on the effects of acid citrate buffers on collagen fibers[13] and by the complete removal of the argyrophilic fibers of the carrageenin granuloma[24] and granulation tissue[25] following extraction of the unfixed tissue with acid citrate buffer.

The insoluble collagen is of fibrillar origin and constitutes the larger proportion of the total collagen of connective tissue. Radioisotope studies with rabbit skin[16] and the carrageenin granuloma of the guinea pig[17] have shown that the turnover rate of insoluble collagen is very low. Similar studies on the rat[26] indicate that the turnover rate of insoluble collagen is low and varies with the source of collagen, being higher in bone and lower in tendon. Its turnover also varies with age, being higher in younger animals. It would be of interest to know the turnover rate of the collagen of the periodontal membrane of continuously erupting teeth as compared to that of teeth with limited growth.

Under certain conditions even insoluble collagen can be broken down relatively fast, as indicated by the rapid disappearance of collagen from the cirrhotic liver of the rat following cessation of the administration of carbon tetrachloride[27] and by the rapid fall of the total collagen content of the uterus following parturition[28].

In summary, the available evidence suggests that the *in vivo* precursor of the collagen fibril is extractable by cold, neutral salt solutions, and is probably of extrafibrillar origin. The citrate extractable and insoluble collagens are of fibrillar origin, the former being an intermediate for only part of the latter.

The mechanism of connective tissue fibril formation. The factors that determine fibril formation and fibril structure have been investigated by *in vitro* experiments on the reconstitution of fibrils from collagen in solution. Such *in vitro* experiments permit adequate control of environmental factors. For fibril reconstitution many collagen solutions have been used, obtained by extracting various types of connective tissue (usually skin and tendon) from different animals (usually calf, rat, guinea pig, rabbit and fish) with cold neutral salt solutions, acid citrate buffers or dilute acetic acid. By altering in various ways the properties of these collagen solutions it has been possible to obtain fibrils exhibiting the normal 640 A° periodicity[29]. It is most interesting that under certain environmental conditions two new structural forms of collagen have been obtained from the above collagen solutions. One of these, called "fibrous long-spacing" (FLS) consists of fibrils with an axial periodicity varying from 1500 A° to 3000 A° (average about 2200 A°). The other type called "segment long-spacing" (SLS) consists of segments 1500 A°-3000 A° (average about 2200 A°). The production of these new structural types has helped in the study of the factors which determine fibril structure. Many methods have been described for the production of fibrils of the 640 A°, FLS and SLS variety[13, 30, 31, 33, 32].

Experiments dealing with the reconstitution of fibrils from collagen solutions pose many questions. First, it would be interesting to know the conditions that determine the precipitation of collagen from solution. Second, when precipitation occurs, why is the precipitate in some cases fibrous and in others amorphous. And finally, whenever a fibrous precipitate is obtained, what are the conditions determining its structure; because in some cases the fibrils are structureless, whereas in others they have a structure which may be of the 640 A°, FLS or SLS variety. The answers to these questions are, indeed, poorly understood. However, from the large number of experiments already performed it appears that the above mentioned processes are regulated by an interplay of pH, ionic strength, negatively charged macromolecules such as chondroitin sulfate, hyaluronate, RNA, DNA, ATP, etc., low molecular weight electrolytes and non-electrolytes such as urea, arginine, ascorbic acid, lysine, Li^+, HCO_3^-, etc., and temperature[35, 34, 30, 32].

The participation of the above factors in the *in vitro* formation of fibrils and in the determination of their structure, strongly suggests that fibril formation and fibril structure are closely related to the electric charge and its distribution on the collagen fibril precursor. These in turn may determine the presence of attractive forces among the particles and the alignment of these particles in certain ways.

Whether the factors influencing fibril formation and fibril structure *in vitro* play a role in the *in vivo* fibrillogenesis is a matter of speculation. The information at present available suggests that a disturbance in the formation and/or structure of connective tissue fibrils may not be due only to an abnormality of the precursor of the collagen fibril, but may also be due to a disturbance in environmental factors. Unfortunately, the study of such environmental factors in connective tissue disturbances, in wound healing, in embryonic growth etc., has been neglected.

The nature of the *in vivo* transformation of the neutral salt extractable collagen into fibrils could be associated with a change in the amino acid composition of this precursor, as, for example, appears to occur in the conversion of fibrinogen to fibrin, or could be physical in nature, such as a change in the state of aggregation of the units of collagen structure. It is most interesting that fibrils with a 640 A° periodicity can be formed *in vitro* not only from solutions of neutral salt extractable collagen, but also from solutions of acid citrate extractable and acetic acid extractable collagen. Such observations suggest that neutral salt extractable collagen is not the only precursor of fibrils in *in vitro* fibrillogenesis, and that the collagen particles of the various collagen fractions may have great similarities. Indeed, physical chemical and chemical studies suggest that they are very similar.

Boedtker and Doty conducted light scattering, viscosity, osmotic pressure and sedimentation studies on solutions of acid citrate extracted collagen from carp swim bladder tunics in acid citrate buffer (pH 3. 7)[36, 37]. Their results indicated the presence of extremely asymmetric, rod-like particles having a diameter of 13.5 A°, a relatively narrow distribution of lengths averaging 3000 A°, an average particle weight of 345,000 and a mass per unit length around 100.

The presence in solution of collagen particles 3000 A° long and 13.5 A° wide is in agreement with recent electronmicroscopic observations. First, particles 15 A° wide and 2200 A° long have been directly visualized by Hall with the electronmicroscope[38]. Second, Gross, Highberger and Schmitt[39] have shown that from a common starting acid solution of ichthyocol, fibrils with normal periodicity, FLS and SLS could be precipitated in separate aliquots almost quantitatively. They also showed that each of these structural forms may be redissolved and converted almost quantitatively into either of the other forms. Based on these two electronmicroscopic observations they postulated that the structural unit of those three types of fibrils produced *in vitro* is a particle whose length is equal to the period of the long spacing forms (2000-3000 A°) and whose width is less than 50 A°. This particle was named tropocollagen and it is interesting to note that its dimensions are similar to those obtained by physical chemical methods for acid citrate extractable collagen.

The participation of tropocollagen particles in *in vivo* fibrillogenesis is still uncertain. The demonstration of tropocollagen particles in the native fibril by application of high resolution electronmicroscopy may be necessary before tropocollagen is considered as the biological unit of structure of the native connective tissue fibrils.

Recent evidence suggests that the various collagen fractions when examined under similar conditions (pH, ionic strength, etc.) exhibit similar physical chemical properties[34, 39a].

In parallel with the studies on the physical chemical properties of the various soluble collagens, studies have also been conducted for the determination of the chemical composition of these proteins[40, 41]. The data indicate that the amino acid composition of all three collagen fractions are essentially the same. There are, however, small differences, such as a higher hydroxyproline and a lower tyrosine content of the citrate extractable collagen as compared to that of neutral salt extractable and insoluble collagen. It is generally assumed that the citrate extractable collagen approaches in composition that of the pure collagen protein, and that the various collagenous fractions obtained all consist basically of this protein, the small differences in composition between them being due to their association with varying amounts of non-collagenous material.

In summary, the available evidence suggests that the particles of the various collagen fractions obtained by the different methods of extraction and believed to be of different morphological origins appear to have similar physical chemical and chemical properties. They can also serve as precursors of fibrils formed *in vitro*. There are, however, two major differences among the particles of the various collagen fractions. First, there are metabolic differences as evidenced by the radioisotope studies[16, 23, 17] which suggest that only neutral salt extractable collagen is the precursor of insoluble collagen in *in vivo* fibrillogenesis. Second, there are differences in solubility, while in their native state. For the extraction of acid citrate extractable collagen from fresh connective tissue a stronger collagen dispersing agent is needed than for the extraction of neutral salt extractable collagen, while insoluble collagen is not solubilized even in an acid milieu. These differences in solubility suggest that the number and strength of the bonds between the particles, while in their native state, are not the same in the various collagen fractions. It appears, that the changes the neutral salt extractable collagen undergoes during the *in vivo* fibril formation and thus during its conversion to acid citrate extractable and insoluble collagen may not involve a change in the amino acid composition of this precursor but may be associated with a change in its state of aggregation resulting from the formation of increasingly more numerous and stronger interparticle cross-links. On the basis of *in vivo* and *in vitro* studies Jackson[17, 42] has proposed the following hypothesis on fibrogenesis. Neutral salt extractable collagen aggregates in the extra-cellular space into a fibrous structure. At this stage no fibers are visible histologically. As development proceeds, the fibrils accumulate further collagen molecules, increasing in length and diameter until they become visible histologically as argyrophil fibers. These fibers probably correspond to citrate soluble collagen. As the fibers increase further in length and thickness, the inner layers become increasingly insoluble owing to the increasing intermolecular crosslinking, while the most recently formed external layers are still extractable with citrate buffers. This process of increased crosslinking extends to the outer layers as the fiber ages, leading to the observed decrease in the proportion of extractable collagen.

The nature of the cross-links of collagen. The cross-links, both within and between the collagen particles, are important in determining the properties of the collagen fibril, such as thermal stability, solubility, etc. It is generally considered that the cohesive forces between the elementary units of the collagen fibrils are of three types: a) salt-like cross-links; b) hydrogen bonds and c) Van der Waals forces.

Hydrogen bonds between the ketoimide groups of adjacent chains are believed to be very common. Recently, Gustafson has offered

evidence for the existence of hydrogen bonds between hydroxy groups and the keto-oxygen of the ketoimide group[2, 43]. The hydroxyproline content of vertebrate collagen is directly proportional to its shrinkage temperature and this suggests that of all the hydroxy groups in collagen the hydroxy group of hydroxyproline is most important for the hydrothermal stability[2]. However, since the collagen of the earthworm cuticle, although very rich in hydroxyproline, has a low shrinkage temperature[6], it appears that factors other than hydroxyproline content play a role in the hydrothermal stability of at least this type of collagen[44].

Besides the direct interaction between collagent particles, there is evidence suggesting that non-collagenous materials (non-collagenous protein, polysaccharides) may contribute in the bonding of collagen particles[45, 46, 47].

Growth and differentiation of connective tissue fibrils. Investigations on fibril formation in tissue culture, in embryonic development and in repair suggest that a fibril once formed undergoes through its lifespan significant changes. These variations include change in width, length, axial periodicity, staining reactions and possibly in the wide-angle diffraction pattern.

First, it appears that during their development the fibrils become wider,[48, 49, 50]. The electron microscope investigations of Schwartz and his associates,[51, 52, 53, 54] on connective tissue fibrils of various organs indicate that during the various stages of embryonic and postnatal development the distribution curves of fibril thickness and the average maximum fibril thickness differ greatly from organ to organ. Similarly the age at which these values become stabilized exhibits organ differences. Observations of this sort are most interesting because they indicate that observations made on the connective tissue of one organ do not necessarily apply to that of another organ.

Second, it appears that during their development the fibrils become longer as evidenced by the electronmicroscopic studies of Banfield[49] on embryonic and adult human dermis.

Third, electronmicroscopic investigations[55, 50] have shown that the first fibrils to appear have a periodicity of 210 A°, while a periodicity of 640 A° becomes evident at later stages. If a change in periodicity occurs it would indicate that during its development the fibril undergoes significant changes related to the arrangement of the collagen particles and/or the polypeptide chains themselves.

Fourth, Randall et al.[55] have reported that the wide angle diffraction pattern of the fibrils changes during their development. If these findings are not the result of contamination with ground substance, they would indicate that in the fibril the attainment of order in the polypeptide chains of the collagen particles is not a sudden, but rather a slow process.

Fifth, during their development the fibrils form bundles and exhibit differences in their staining reactions. This subject is closely associated to the differences between reticular and collagenous fibers. Collagen fibers are the fibers of the white fibrous tissue. Reticular fibers occur wherever connective tissue forms a boundary with other structures such as epithelia blood vessels etc. They also form a network in reticular tissue (lymphnode, bone marrow etc.) In all the above locations the reticular fibers are believed to exist as permanent structures. Reticular fibers can also be seen in the granulation tissue of healing wounds and in certain areas of the developing embryo where they appear to be converted to or replaced by collagen fibers.

There are distinct differences between reticular and collagen fibers. First, there are the well known morphological differences as seen in the light microscope and differences in their staining reactions with the silver stain and the Van Gieson method[57, 58, 25]. Second, there are histochemical differences. Reticular fibers are strongly PAS positive[59] and metachromatic following sulphation[60, 61] while collagen fibers stain less intensely with the PAS method and are orthochromatic following sulphation[60,61]. The stainability of both types of fibers by both methods does not seem to be affected by prior treatment with amylase or hyaluronidase or by prior pyridine extraction. These histochemical findings indicate that there is a difference in the

chemical make-up between collagen and reticular fibers but they do not offer any suggestion as to the nature of this difference. It could be quantitative, qualitative or a change in the spatial arrangement of the component substances. If, as Bangle and Alford[62] suggested, the PAS reaction of collagen is due to associated nonglucosamine polysaccharide, then the difference between collagenous and reticular fibers may be due to some change of this material.

Third, chemical analytical investigations indicate that there are differences in chemical composition between reticular and collagen fibers. Windrum, Kent and Eastoe[63] analyzed the reticular fibers of the subcortical tissue of the kidney and found that this material consisted of 85 per cent protein having an amino acid composition simliar to that of collagen protein, 4.2 per cent carbohydrate consisting of galactose, mannose, fucose and small amounts of hexosamine, but free of uronic acid and sulphate ester, and 10.9 per cent bound fatty acids of which 95 per cent was myristic acid. On the other hand, collagen fibers contain not more than 1 per cent carbohydrate consisting mainly of galactose, glucose, mannose and hexosamine[9,64,65]. Since the noncollagenous components associated with collagen or reticular fibers have not yet been isolated and characterized it cannot be stated with certainty if there are any qualitative differences between the non-collagenous components of these two tpes of fibers. It appears, however, that quantitative differences do exist, the reticular fibers being associated with much larger amounts of non-collagenous components. It is interesting to note, that the non-collagenous components associated with reticular and collagen fibers are free of uronic acid, which suggests that the carbohydrate moiety is not an acid polysaccharide.

Fourth, the immunological studies of Cruickshank and Hill[66] suggest that reticular fibers contain an antigen, probably a polysaccharide, which is either absent from collagen fibers or is present in a modified form. These findings do suggest that a qualitative difference may exist between the non-collagenous components of the two types of fibers.

Fifth, studies by polarized light of collagenous fibers and of reticular fibers from various sources including granulation tissue, indicate the presence in reticular fibers of a component, probably of non-collagenous nature, the molecules of which are arranged perpendicularly to the fiber axis. In collagenous fibers this component is either absent or not arranged perpendicularly[67]. These findings are consistent with a qualitative difference or a difference in spatial arrangement between the non-collagenous components of reticular and collagenous fibers.

There are, however, similarities between reticular and collagenous fibers. The amino acid composition of the collagen protein component is similar in both fibers[63]. Reticular fibers from various sources exhibit a 640 A° periodicity[58, 68, 69, 70]. Reticular fibers from human kidney[71] and dermis of the new born rat[69, 70] give an x-ray diffraction pattern characteristic of collagen. Finally both types of fibers are resistant to the action of trypsin or testicular hyaluronidase, but are rapidly lysed by pepsin or collagenase.

In view of the similarities and differences between reticular and collagenous fibers and the presence in granulation tissue and certain areas of the connective tissues of the embryo or reticular fibers which are eventually transformed to or replaced by collagen fibers, it is important to consider the nature of this transformation or replacement. The fibrils of the human cornea and sclera[52], Achilles tendon[51] and skin[53] have been examined during various stages of their embryonic and post-natal development with the electron-microscope following silvering with the Gomori method or the periodic acid silver tetramine technique. In the case of the sclera, for instance, it was found that the mode of silvering changed during the various stages of development. It is of interest to note that the final stage in the mode of silvering was not arrived at by the fibrils of all organs; in some organs the development of the fibrils stopping at an earlier stage. The above findings indicate that during their development the fibrils undergo changes, but the difficulty arises in the interpretation of the

nature of these changes. An understanding of the nature of such changes presupposes an understanding of the nature of argyrophilia. The chemical basis of silver impregnation is unknown. It does not seem that argyrophilia depends on physical factors, such as the thinness of fibrils[72]. Most likely, as the studies of Irving and Tomlin have suggested, it depends upon the non-collagenous material, this is the cement substance, in which the fibrils are embedded[68]. The chemical basis of the periodic acid silver tetramine technique is better understood. Most likely aldehydes produced by the periodic acid oxidation cause the reduction of silver. The changes observed indicate that during the development of the fibrils there is a change in the location of the reduction sites. Whether these sites belong to the collagen protein component of the fibril, such as the hydroxylysine residues, to the associated cement substance or both cannot be ascertained at the present time. A change in the associated cement substance is likely and is supported by the above mentioned histochemical, chemical and immunological studies, the studies with polarized light and the work of Irving and Tomlin.

The apparent conversion of certain types of reticular fibers to collagenous fibers is associated with changes in the ground substance. In the developing skin of the pig the appearance of collagenous fibers is accompanied by a relative increase in chondroitin sulphate B[73], while in healing wounds it is associated with a decrease in the intensity of metachromasia, a reduction in the area occupied by metachromatic material and a decrease in the concentration of hexosamine[74, 75]. Whether the appearance of collagenous fibers is causally related with the above changes in the ground substance remains to be seen.

The fact that argyrophilia is shared by all reticular fibers is perhaps the most important factor for the widely held opinion that all reticular fibers are identical. It is unlikely that argyrophilia is specific enough to establish identity, especially since it has been shown that not one but many different substances can render collagenous fibers argyrophilic[68]. Recent investigations strongly suggest that all reticular fibers are not identical. The reticular fibers found in embryonic and regenerating areas of connective tissue lose their argyrophilic properties following extraction with neutral salt solutions and are removed almost completely following extraction with an acid citrate buffer[24, 25, 76, 77], while the reticular fibers of basement membranes and of the lymph-reticular tissue are not affected by the above mentioned extracting solutions[25, 76, 77]. The first group of fibers is ultimately converted to or replaced by collagen fibers and may, therefore, be considered as "precollagenous," while the fibers of the second group appear to exist as permanent structures and may, therefore, be considered as a branch line rather than as being on their way to conversion to collagen fibers. The basis for the differences in the solubility properties of these two groups of reticular fibers is unknown.

In summary, the connective tissue fibrils undergo during their development an increase in width and length, a change in their axial periodicity and possibly their X-ray diffraction pattern, and aggregate to form bundles which are visible with the light microscope. Histochemical, chemical and electronmicroscopic studies and studies with polarized light suggest that the conversion of reticular fibers found in embryonic and regenerating areas of connective tissue to collagenous fibers is accompanied by a decrease in the amount of associated cement substance. A qualitative change in this cement substance or a change in the spatial arrangement of its components may also be involved in this conversion, while a change in the collagen component of the fibrils other than an increasing crosslinking between the collagen particles cannot be excluded. There is evidence to suggest that basement membrane reticulin and the reticlin of developing connective tissue are not identical.

The non-collagenous material in which the fibrils are embedded, that is the cement substance, is believed to consist of polysaccharide-protein complexes. The nature of the bonds between the polysaccharide and the protein and between the collagen protein and the complex

is poorly understood. Electronmicroscopy combined with highly refined methods of histochemistry may eventually elucidate not only the nature of these substances but also their localization at the various levels of organization of the collagenous fiber. There is evidence to suggest that these complexes play an important role in determining the properties of the collagenous fiber. For example, Jackson observed that treatment of calf tendon with hyaluronidase increased its swelling and solubility in dilute acetic acid and reduced its shrinkage temperature[45]. Similarly, Gross observed that the presence of non-collagenous material during *in vitro* reconstitution of fibrils decreased the solubility of the fibrils formed[78].

At this point it seems appropriate to turn to the collagen fibril precursor and to examine the cells responsible for its formation, along with the cell organelles and the biosynthesis of the collagen molecule.

The cell and fibrillogenesis. Evidence presented by histological and electronmicroscopic examination of collagen fibril formation during repair and embryonic development and especially studies on fibril formation in tissue culture have led to the general acceptance of the fibroblast, osteoblast and chondroblast as the cells responsible for the synthesis of collagen or its precursors[79, 80, 48, 81, 12, 82].

Granules of the order of 1 micron have been demonstrated within the cytoplasm of fibrogenic cells. Various cytochemical methods have been applied on fixed preparations to elucidate the chemical nature of these granules. They have been shown to be PAS positive and this reaction is not affected by prior extraction of lipid or digestion with hyaluronidase or amylase[83, 84, 48, 12]. PAS positive granules removable with amylase have been shown to be present in immature umbilical cords[85]. The granules are also Hale positive[12, 48] and metachromatic when stained supravitally with toluidine blue[48, 86, 87, 88]. In fixed preparations metachromatic granules have been demonstrated which are removable with ribonuclease[89]. However, staining with methods specific for RNA and DNA failed to reveal the presence of such material in the granules[86, 90]. The granules exhibit sulfation metachromasia which is not affected by prior extraction of lipids, digestion with amylase or hyaluronidase, but is removed by beta-glucuronidase[91, 85]. On the basis of these observations Schoenberg and Moore concluded that the granules contain a carboxylated but not sulphated tri- or tetrasaccharide having glucuronic acid in its non-reducing end[85]. Granule preparations isolated by differential centrifugation of sucrose homogenates of osteoblast cultures were found to consist of polysaccharide containing hexosamine, and of protein containing small amounts of hydroxyproline[90].

The above mentioned histochemical and chemical data, the presence of these granules only during the period when elaboration of extracellular material[48] would be expected and the high rate of incorporation of ^{14}C-L-proline by these granules[92] suggest that they may be the sites of elaboration of collagen protein and polysaccharide.

The question whether fibrils are formed intra- or extracellularly is still a matter of controversy. Intracytoplasmic fibrils have been observed with the electronmicroscope within fibrogenic cells during the period when elaboration of extracellular material would be expected[50, 80, 93, 48, 81]. However, the diffuseness of the cell margin makes it difficult to decide whether a fibril is located within, at the surface or outside the cell. While the possibility that intracellular collagen exists in fibrous form needs further investigation, there is evidence to suggest that fibrogenic cells deliver collagen in a non-fibrous form. The observation that the fibrils of the developing avian tendon increase in width at the expense of the interfibrillar material[48] suggests that this material may contain collagen in a non-fibrous form originating from the cells. Whether the non-fibrous collagen produced by the cell is secreted in the form of neutral salt extractable collagen, believed to be the *in vivo* precursor of the collagen fibril, or in a relatively simpler form remains to be seen.

The biosynthesis of collagen. The biosyn-

thesis of the collagen protein presents all the complexities and difficulties associated with protein synthesis. Collagen is unique in that it is the only protein (with the exception of elastin) that contains hydroxyproline and hydroxylysine and, therefore, several studies have been made related to the incorporation of these amino acids. Radioisotope studies with labelled hydroxyproline, proline, hydroxylysine and lysine[94, 95, 96, 97, 98, 99, 100] have lead to the suggestion that the cell cannot utilize free hydroxyproline or hydroxylysine for collagen synthesis, and that these amino acids are derived by the hydroxylation of proline or lysine. It has also been stated that the hydroxylation of these amino acids occurs while they are already in peptide linkage[94]. If the formation of hydroxylysine and hydroxyproline from lysine and proline respectively is not simultaneous or nearly simultaneous with the incorporation of both amino acids into collagen, but instead occurs at a slow rate, it would mean that a whole series of intermediates, ranging from completely unhydroxylated to fully hydroxylated, would be formed. A poorly hydroxylated precursor has not yet been isolated, but it may be that the techniques used for isolation of collagen are not suitable for the isolation of such a precursor.

GROUND SUBSTANCE

The term ground substance is used in different senses, but from a morphological point of view it may be appropriate to use Dorfman's definition as "the amorphous (to the limits of resolution of the electronmicroscope) continuous existing between the cells and vascular system"[101]. Ground substance is abundant during embryonic development and during repair, but then decreases in volume in most vascularized mesenchymal tissues parallel with the increasing amounts of fiber structures. There are, however, some exceptions in the avascular connective tissues (cartilage, cornea, etc.), for these contain large amounts of ground substance, even in adults.

THE CHEMISTRY OF THE GROUND SUBSTANCES

The composition of the ground substances has been investigated mainly by histochemical methods and chemical isolation methods. Both of these have their limitations. Present histochemical methods have only limited specificity, do not lend themselves to quantitative estimations and a negative result does not imply absence of the material, but rather non-availability of the reactive groups. They have, however, the advantage of giving information about the histological localization of the reactive groups. Chemical isolation methods although superior for qualitative and quantitative estimations require large samples and fail to give information on the relationship between the substances isolated and histologically defined structures. Indeed, there is no direct evidence and it is only assumed that the hyaluronic acid and chondroitin sulphate isolated from adult skin come from the ground substance rather than other histologically defined elements.

The ground substance is not a uniform chemical substance, but is made up of a variety of components of diverse origins. The composition of the ground substance can be considered as follows:

1. Substances derived from the blood stream, such as water, inorganic ions, glucose, blood proteins, etc.
2. Metabolic products of parenchymal cells.
3. Metabolic products peculiar to connective tissue, such as certain mucopolysaccharides and soluble collagens.

Of all the polysaccharides assumed to be present in the ground substance the acid mucopolysaccharides have been most extensively examined, because they have been isolated and, in some cases, their structure determined. They are divided into non-sulphated mucopolysaccharides, such as hyaluronic acid and chondroitin, and sulphated mucopolysaccharides, such as chondroitin sulphate A, B, and C, heparitin sulphate and keratosulphate[102, 103, 104].

The total acid mucopolysaccharide content, the type of acid mucopolysaccharides present and their distribution patterns exhibit great differences from organ to organ. On this basis, the various organs have been divided into at least seven groups[102, 104]. The reasons for such differences are unknown. Whether there is a causal relationship between the differences in

the types and distribution patterns of the acid mucopolysaccharides in the various types of connective tissue and the types of fibrous structures present in these areas remains to be seen.

Although the acid mucopolysaccharides have been most extensively studied, evidence has been accumulating that connective tissue contains significant amounts of heteropolysaccharides which do not contain uronic acid. Carbohydrate fractions free of uronic acid have been obtained from human subcutaneous tissue[105], the vitreous body[106, 107] and many other sources[108, 109, 110, 111, 63]. The individual polysaccharides of which these fractions consist have not yet been isolated. Recent histochemical observations on umbilical cord[112] and granulation tissue[91] using the sulphation metachromasia method are consistent with the above chemical findings. Not sufficient attention has been paid to these types of connective tissue polysaccharides, and it is likely that the interpretation of the findings of many studies may have suffered because of this.

Data on synovial fluid[113, 114, 115, 116], cartilage[117, 118, 119, 120], skin[121, 23, 40], and other organs[110] indicate that the connective tissue contains non-collagenous proteins. Following extraction of mesenchymal tissues under mild conditions the polysaccharides are mostly obtained as complexes with non-collagenous proteins. Treatment of hyaluronic acid protein complexes from human and ox synovial fluid and human umbilical cord with papain or plasmin results in reduction of viscosity and particle size and in the production of abnormal mucin clots[113, 114, 116, 120, 117]. Such observations suggest that the protein moiety may play an important role in the properties of the complex and that abnormalities in the ground substance may be the result of changes in the proteins.

THE ORIGIN OF THE GROUND SUBSTANCE MATERIALS

It may safely be assumed that water and electrolytes are derived from the blood, while proteins, peptides and amino acids, and collagen precursors are derived from the protein pool and the fibrogenic cells respectively.

The origin of the mucopolysaccharides of the ground substance has been a subject of extensive speculation for years. Both the mast cell[122, 123] and the fibroblast have been proposed. The evidence at present available is more in favor of the fibroblast producing connective tissue mucopolysaccharides, other than heparin and related compounds. First, fibroblasts grown in tissue culture are capable of synthesizing hyaluronic acid and chondroitin sulfuric acid[124]. Second, there is a close correlation between fibroblastic activity and the production of mucopolysaccharides during wound healing and embryonic development[125, 75], while mast cells fail to show such a correlation[75, 126]. Finally, histochemical investigations have shown that the metachromatic material of mast cells is resistant to hyaluronidase[127], in contrast to that of granulation tissue.

The controversy about the fibroblast and the mast cell as the possible source of the connective tissue mucopolysaccharides may be of academic interest if mast cells originate from fibroblasts. It may be interesting to note that sulphated hyaluronic acid or compound 48/80—heparin complex, is ingested by the fibroblasts which are then morphologically similar to mast cells[129, 130]. It may be that not one but all connective tissue cells, including the capillary endothelial cell, participate in the formation of connective tissue mucopolysaccharides[131].

The function of the ground substances. The localization and the structure of the majority of connective tissue mucopolysaccharides is unknown. Similarly, only a few physicochemical studies of mucopolysaccharides in their native state have been conducted. For these reasons, their functions are poorly understood. The structure of hyaluronic acid as a highly hydrated coiled sphere and its easy deformation explain its function in water binding and as a lubricant. The chondroitin sulphates are capable of binding cations and may be of significance in the distribution and storage of extracellular cations. It has been suggested that the function of chondroitin sulphate may be similar to that of an ion exchange resin[132].

There is evidence suggesting that acid muco-

polysaccharides participate in detoxifixation mechanisms by binding with basic substances released from injured cells. The resulting complex may then be ingested by fibroblasts[130].

Acid mucopolysaccharides have been implicated in fibrillogenesis. This is based on the observation that during wound healing and the embryonic development of connective tissue acid mucopolysaccharides accumulate prior to the formation of collagen fibers[73, 74, 75, 133]. Furthermore, collagen fibrils can be reconstituted by the addition of acid mucopolysaccharides to solutions of soluble collagens[33, 30]. However, the action of acid mucopolysaccharides on the reconstitution of collagen fibrils has been shown to be non-specific[134], and collagen fibrils have been reconstituted in the absence of uronic acid containing carbohydrate[135]. The role of acid mucopolysaccharides in *in vivo* fibrillogenesis is unknown. Gross maintains that collagen particles are "spontaneously precipitated in the form of collagen-type fibril because of the characteristics of the ionic environment". He suggests that the role of the non-collagenous components of ground substance may be "to provide the necessary viscous, even thixotropic, medium required to keep the precipitated fibrils localized to specific areas and arranged in a particular pattern; the fibrils might otherwise precipitate in a tangled mass around the cells[135]."

The increased solubility in acetic acid and decreased thermal shrinkage temperature of tendon following hyaluronidase treatment[45] has suggested that chondroitin sulphate is important in the stability of collagen fibers. Meyer has stated that the chondroitin sulphates are probably in intimate contact with the fibrous elements and actually may form part of the fibrous structures[136]. It is interesting to note that purified collagen is free of uronic acid.

SUMMARY

Connective tissue consists of three main elements: cells, fibers and ground substance. Quantitative and qualitative differences among these three elements give rise to the varieties of connective tissue, such as fibrous connective tissue, bone, dentin, etc.

The fibroblast, the osteoblast and the chondroblast are believed to be instrumental in the production of collagen and of the ground substance mucopolysaccharides. The available evidence suggests that these substances are delivered by the cell in a precursor form, which then undergoes changes in the intercellular spaces. The nature of the precursors delivered by the cell is at present a matter of speculation.

Today three collagen fractions are recognized: (a) neutral salt extractable collagen; (b) acid citrate extractable collagen, and (c) insoluble collagen. The latter two collagen fractions appear to be of fibrillar origin, while the first is believed to be of extrafibrillar origin. Neutral salt extractable collagen is considered to be the *in vivo* precursor of the collagen fibril. Environmental factors such as pH, ionic strength, negatively charged macromolecules and temperature are instrumental in the formation and structure of the fibril. It is believed that the changes the neutral salt extractable collagen undergoes during the *in vivo* fibril formation, and thus during its conversion to acid citrate extractable and to insoluble collagen, may be associated with a change in its state of aggregation resulting from the formation of increasingly more numerous and stronger interparticle crosslinks. This suggestion is consistent with the close similarity in physical chemical and chemical properties of the various collagen fractions, with the differences in their solubility properties while in their native state, and with the observation that typical collagen fibrils can be reconstituted *in vitro* from all collagen fractions. Besides the increasing crosslinks between collagen particles, there is evidence to suggest that changes in the associated cement substance are also involved during the formation and growth of the fibrils. These changes may be closely related to the conversion of reticular fibers found in embryonic and regenerating areas of connective tissue to collagenous fibers.

The ground substance is not a uniform chemical substance, but is made up of a variety of components of diverse origins. The acid mucopolysaccharides have been most extensively studied, but it appears that the greatest proportion of connective tissue polysaccharides is free

of uronic acid. The components of the ground substance play important roles in water binding, in the distribution and storage of extracellular cations, in detoxification mechanisms, in the properties of the collagenous fiber and possibly in fibrillogenesis.

The cells, the fibers and the ground substance of connective tissue are three closely interrelated and interdependent elements. The fact that nutrients from the blood and metabolic products from the cells must pass through connective tissue, emphasizes the importance of this tissue in health and disease.

4001 Spruce Street,
Philadelphia 4, Pennsylvania

BIBLIOGRAPHY

1. Rudall, K. M.: The Distribution of Collagen and Chitin., Symp. Soc. Exper. Biol. IX., New York, Academic Press, Inc., 1955, p. 49
2. Gustavson, K. H.: The Function of Hydroxyproline in Collagen. Nature 175:70, 1955.
3. Gustavson, K. H.: Hydroxyproline and Stability of Collagen. Acta. Chem. Scand., 8:1298, 1954.
4. Reed, R. and Rudall, K. M.: Electronmicroscope Studies on the Structure of Earthworm Cuticle. Biochem. Biophys. Acta, 2:7, 1948.
5. Randall, J. T.: Aspects of Macromolecular Orientation in Collagenous Tissues. J. Cell. Comp. Physiol., Suppl. I., 49:113, 1957.
6. Singleton, L.: The Chemical Structure of Earthworm Cuticle. Biochem. et. Biophys. Acta., 24:67, 1957.
7. Stack, M. V.: The Chemical Nature of the Organic Matrix of Bone, Dentin, and Enamel. Ann. N. Y. Acad. Sci., 60:585, 1955.
8. Bowes, J. H. and Kenton, R. H.: The Aminoacid Composition and Titration Curve of Collagen. Biochem. J., 43:358, 1948.
9. Schmitt, F. O., Gross, J. and Highberger, J. H.: States of Aggregation of Collagen. Symposia Soc. Biol. IX, New York, Academic Press, Inc., 1955, p. 148.
10. Bear, R. S.: The Structure of Collagen Fibrils. In Advances in Protein Chemistry. 7:69. New York, Academic Press, Inc. 1952.
11. Rich, A. and Crick, F. H. C.: The Structure of Collagen. In Stainsby, G. Ed.: Recent Advances in Gelatin and Glue Research. New York, Pergamon Press, 1958, p. 20.
12. Jackson, S. F. and Smith, P. H.: Studies on the Biosynthesis of Collagen I. The Growth of Fowl Osteoblasts and the Formation of Collagen in Tissue Culture. J. Biophys. and Biochem. Cytol., 3:897, 1957.
13. Gross, J., Highberger, J. H. and Schmitt, F. O.: Extraction of Collagen from Connective Tissue by Neutral Salt Solutions. Proc. Natl. Acad. Sci., 41:1, 1955.
14. Jackson, D. S. and Fessler, J.: Isolation and Properties of Collagen Soluble in Salt Solution at Neutral pH. Nature, 176:69, 1955.
15. Orekhovitch, V. N., Stanowski, A. A. and Plotnikova, N. E.: Isolation of Crystalline Proteins of a New Type (procollagen) from Various Organs of the Vertebrates. Chem. Abstr., 43:259, 1949.
16. Harkness, R. D., Marko, A. M., Muir, H. M. and Neuberger, A.: Precursors of Skin Collagen In Randall, J. T. Ed.: Nature and Structure of Collagen. New York, Academic Press Inc., 1953, p. 208.
17. Jackson, D. S.: The Formation and Breakdown of Connective Tissue. In Tunbridge, R. E. Ed.: C.I.O. M.S. Symposium on Connective Tissue., p. 62-74, Springfield, Ill., C. C. Thomas, 1957.
18. Gross, J.: Studies on the Fibrogenesis of Collagen. Some Properties of Neutral Extracts of Connective Tissue. In Tunbridge, R. E. Ed.: C.I.O.M.S. Connective Tissue A Symposium. Springfield, Ill., C. C. Thomas, 1957, p. 45.
19. Gross, J.: Studies on the Formation of Collagen. II. The Influence of Growth Rate on Neutral Salt Extracts of Guinea Pig Dermis. J. Exper. Med., 107: 265, 1958.
20. Gross, J.: Studies on the Formation of Collagen. I. Properties and Fractionation of Neutral Salt Extracts of Normal Guinea Pig Connective Tissue. J. Exper. Med., 107:247, 1948.
21. Orekhovitch, V. N.: 2nd Int. Congr. Biochem. Communications, p. 106, 1952.
22. Orekhovitch, V. N.: 3rd Int. Congr. Biochem. Communications, p. 50, 1955.
23. Harkness, R. D., Marko, A. M., Muir, H. M., and Neuberger, A.: The Metabolism of Collagen and Other Proteins of the Skin of Rabbits. Biochem, J., 56: 558, 1954.
24. Jackson, D. S. and Williams, G.: Nature of Reticulin. Nature, 178:915, 1956.
25. Robb-Smith, A. H. T.: What is Reticulin? In Tunbridge, R. E. Ed.: C.I.O.M.S. Connective Tissue. A Symposium. Springfield, Ill., C. C. Thomas, 1957, p. 177.
26. Slack, H. G. B.: Metabolism of Collagen in the Rat. In Randall, J. T.: Nature and Structure of Collagen. New York, Academic Press, Inc., 1953, p. 51.
27. Cameron, G. R. and Karunaratne, W. A. E.: Carbon Tetrachloride Cirrhosis in Relation to Liver Regeneration. J. Path. Bact., 42:1, 1936.
28. Harkness, M. L. R. and Harkness, R. D.: The Collagen Content of the Reproductive Tract of the Rat During Pregnancy and Lactation. J. Physiol., 123:492, 1954.
29. Schmitt, F. O., Hall, C. E. and Jacus, M. A.: Electron Microscopy Studies on Collagen. J. Cell. Comp. Physiol., 20:11, 1942.
30. Highberger, J. H., Gross, J. and Schmitt, F. O.: The Interaction of Muco-protein with Soluble Collagen; An Electron Microscope Study. Proc. Natal. Acad. Sci., 37:286,1951.
31. Highberger, J. H., Gross, J. and Schmitt, F. O.: Electronmicroscope Observations on Certain Fibrous Structures Obtained from Connective Tissue Extracts. J. Amer. Chem. Soc., 72:3321, 1950.
32. Schmitt, F. O., Gross, J. and Highberger, J. H.: A New Particle Type in Certain Connective Tissue Extracts. Proc. Natl. Acad. Sci., 39:459, 1953.
33. Jackson, S. F. and Randall, J. T.: The Reconstitution of Collagen Fibrils from Solution. In Randall, J. T.: Nature and Structure of Collagen. p. 181, New York, Academic Press, Inc., 1953.
34. Gross, J. and Kirk, D.: The Heat Precipitation of Collagen from Neutral Salt Solutions: Some Rate-regulating Factors. J. Biol. Chem., 233:355, 1958.
35. Porter, K. R. and Vanamee, P.: Observations with the Electronmicroscope on the Solvation and Reconstitution of Collagen. J. Exper. Med., 94:255, 1951.
36. Boedtker, H., and Doty, P.: On the Nature of the Structural Element of Collagen. J. Amer. Chem. Soc., 77:248, 1955.
37. Boedtker, H. and Doty, P.: The Native and Denatured States of Soluble Collagen. J. Amer. Chem. Soc., 78:4267, 1956.
38. Hall, C. E.: A Method for the Observation of Macromolecules with the Electron Microscope Illustrated with Micrographs of DNA. J. Biophys. Ciochem. Cytol., 2:625,1956.
39. Gross, J. Highberger, J. H. and Schmitt, F. O.: Collagen Structures Considered as States of Aggregation of a Kinetic Unit. The Tropocollagen Particle, Proc. Natl. Acad. Sci., 40:679, 1954.
39a. Orekhovitch, V. N. and Shpikiter, V. O.: Procollagens as Biological Precursors of Collagen and the Physiochemical Nature of these Proteins. In Tun-

bridge, R. E. Ed: Connective Tissue. A Symposium. Springfield, Ill., C. C. Thomas, 1957, p. 281.
40. Bowes, J. H., Elliott, R. G. and Moss, J. A.: The Composition of Some Protein Fractions Isolated from Bovine Skin. In Tunbridge, R. E. Ed.: C.I.O.M.S. Connective Tissue Symposium, Springfield, Ill. C. C. Thomas, 1957, p. 264.
41. Jackson, D. S., Leach, A. A. and Jacobs.: The Amino Acid Composition of the Collagen Fractions of Rabbit. Biochem. Biophys., Acta, 27:418, 1958.
42. Jackson, D. S.: Some Biochemical Aspects of Fibrogenesis and Wound Healing. New Eng. J. Med., 259:814, 1958.
43. Gustavson, K. H.: Evidence for the Presence of the -OH . . . OC-Link in Collagen from the Fixation of Non-ironic Chromium Complexes. Acta. Chem. Scand., 9:1049, 1955.
44. Gustavson, K. H.: See Discussion. C.I.O.M.S. Connective Tissue. A Symposium. Springfield, Ill., C. C. Thomas, 1957, p. 206.
45. Jackson, D. S.: Chondroitin Sulfate as a Factor in the Stability of Tendon. In Randall, J. T. Ed.: Nature and Structure of Collagen. New York, Academic Press, Inc., 1953, p. 177.
46. Partridge, S. M.: The Chemistry of Connective Tissue I. The State of Combination of Chondroitin Sulphate in Cartilage. 43:387, 1948.
47. Bowes, J. H., Elliott, R. G. and Moss, J. A.: Some Differences in the Composition of Collagen and Extracted Collagens and Their Relation to Fibre Formation and Dispersion. In Randall, J. T. Ed.: Nature and Structure of Collagen. New York, Academic Press, Inc., 1953, p. 199.
48. Jackson, S. F.: The Morphogenesis of Avian Tendon. Proc. Roy. Soc. B., 144:566, 1956.
49. Banfield, W. G.: Width and Length of Collagen Fibrils During the Development of Human Skin, in Granulation Tissue and in the Skin of Adult Animals. J. Gerontol., 10:13, 1955.
50. Porter, K. R.: Repair Processes in Connective Tissue. Second Conference on Connective Tissues. New York, Josiah Macy, Jr. Foundation, 1951.
51. Pahlke, G.: Elektronenmikroskopische Untersuchungen an der Intersellular substanz des menschlichen Sehnengewebes. Z.f. Zellforsch, 39:421, 1954.
52. Schwartz, W.: Elektronenmikroskopische Untersuchungen uber die Differenzierung der Cornea und Sklerafibrillen des Menschen. Z. Zellforsch, 38:78, 1954.
53. Linke, K. W.: Elektronenmikroskopische Untersuchung uber die Dicerenzierung der Interzellular substanz des Menschlichen Lederhaut. Z. Zellforsch. 42:331, 1955.
54. Schwartz, W.: Morphology and Differentiation of the Connective Tissue Fibers. In C.I.O.M.S. Connective Tissue. A Symposium. Springfield, Ill., C. C. Thomas, 1957, p. 144.
55. Randall, J. T. et. al.: Aspects of Collagen Structure. Nature, 169:1029, 1952.
56. Jackson, D. S.: The Formation and Removal of Collagen in the Carrageenin Granuloma. Biochem. J., 64:8 p., 1956.
57. Jacobson, W.: Histological Survey of the Normal Connective Tissue and its Derivatives. In Randall, J. T. Ed.: Nature and Structure of Collagen. New York, Academic Press, Inc., 1953, p. 6.
58. Kramer, H. and Little, K.: Nature of Reticulin. In Randall, J. T. Ed.: Nature and Structure of Collagen. New York, Academic Press, Inc., 1953, p. 33.
59. Lilie, R. D.: Reticulum Staining with Schiff Reagent After Oxidation by Acidified Sodium Periodate. J. Lab. Clin. Med., 32:910, 1947.
60. Kramer, H. and Windrum, G. M.: Metachromasia after Treating Tissue Sections with Sulfuric Acid. J. Clin. Path., 6:239, 1953.
61. Kramer, H. and Windrum, G. M.: Sulfation Techniques in Histochemistry with Special Reference to Metachromasia. J. Histochem. Cytochem., 2:196, 1954.
62. Bangle, R. and Alford, W. C.: The Chemical Basis of the Periodic Acid Schiff Reaction of Collagen Fibers with Reference to Periodate Consumption by Collagen and by Insulin. J. Histochem. Cytochem., 2:62, 1954.
63. Windrum, G. M., Kent, P. W. and Eastoe, J. E.: The Constitution of Human Renal Reticulin. Brit. J. Exper. Path., 36:49, 1955.
64. Grassman, W. et al.: Electron Microscope and Chemical Studies of the Carbohydrate Groups of Collagen. In Tunbridge, R. E. Ed.: C.I.O.M.S. Connective Tissue. A Symposium. Springfield, Ill., C. C. Thomas, 1957, p. 157.
65. Beck, J.: The Carbohydrate in Collagen. J. Am. Chem. Soc., 63:1483, 1941.
66. Cruickshank, B. and Hill, A.G.S.: Histochemical Identification of a Connective Tissue Antigen. In Randall, J. T. Ed.: Nature and Structure of Collagen. New York, Academic Press, Inc., 1953, p. 27.
67. Brewer, D. B.: Difference in the Fine Structure of Collagen and Reticulin as Revealed by the Polarizing Microscope. J. Path. Bact., 74:371, 1957.
68. Irving, E. A. and Tomlin, S. G.: Collagen, Reticulum and Their Argyrophilic Properties. Proc. Roy. Soc. B., 142:113, 1954.
69. Gross, J.: A Study of the Ageing of Collagenous Connective Tissue of Rat Skin with the Electronmicroscope. Am. J. Path., 26:708, 1950.
70. Gross, J.: Connective Tissue Fine Structure and Some Methods for its Analysis. J. Gerontol., 5:343, 1950.
71. Little, K. and Windrum, G. M.: A Lipid Component of Reticulin. Nature, 174:789, 1954.
72. van der Hoof, A.: A Few Remarks on Connective Tissues Rich in Mucoid. In Tunbridge, R. E. Ed.: C.I.O.M.S. Connective Tissue. A Symposium. Springfield, Ill., C. C. Thomas, 1957, p. 172.
73. Loewi, G. and Meyer, K.: The Acid Mucopolysaccharides of Embryonic Skin. Biochem. Biophys. Acta., 27:453, 1958.
74. Dumphy, E. J., and Udupa, K. N.: Chemical and Histochemical Sequences in the Normal Healing of wounds. New England J. Med., 253:847, 1955.
75. Taylor, H. E. and Saunders, A. M.: The Association of Metachromatic Ground Substance and Fibroblastic Activity in Granulation Tissue. Am. J. Path., 33:527, 1957.
76. Robb-Smith, A.H.T.: The Relationship of Reticulin to Other "Collagens". In Stainsby, G.: Recent Advances in Gelatin and Glue Research. New York Pergamon Press, 1958, p. 38.
77. Robb-Smith, A. H. T.: The Reticulin Riddle. J. Mt. Siani Hosp., 24:1155, 1957.
78. Gross, J.: Studies on the Formation of Collagen III. Time-Dependent Solubility Changes of Collagen *in vitro*. J. Exper. Med., 108:215, 1958.
79. Stearns, M. L.: Studies on Development of Connective Tissue in Transparent Chambers in Rabbits' Ear. Amer. J. Anat., 66:133, 1940. 67:55, 1940.
80. Wasserman, F.: Fibrillogenesis in the Regenerating Rat Tendon with Special Reference to Growth and Composition of the Collagenous Fibril. Amer. J. Anat., 94:399, 1954.
81. Jackson, S. F.: The Formation of Connective and Skeletal Tissues. Proc. Roy. Soc. B., 142:536, 1954.
82. Porter, K. R. and Vanamee, P.: Observations on the Formation of Connective Tissue Fibers. Proc. Soc. Exper. Biol. and Med., 71:513, 1949.
83. Gersh, I. and Catchpole, H. R.: The Organization of Ground Substance and Basement Membrane, and its Significance in Tissue Injury, Disease and Growth. Amer. J. Anat., 85:457, 1949.
84. Heller-Steinberg, M.: Ground Substance, Bone Salts and Cellular Activity in Bone Formation and Destruction. Amer. J. Anat., 89:347, 1951.
85. Schoenberg, M. D. and Moore, R. D.: Studies on Connective Tissue. III. Enzymatic Studies on the Formation and Nature of the Carbohydrate Intermediate of the Connective Tissue Polysaccharides in Human Umbilical Cord. A.M.A. Arch. Path., 65:115, 1958.
86. Jackson, S. F.: Cytoplasmic Granules in Fibrogenic Cells. Nature, 175:39, 1955.
87. Grossfeld, H.: Metachromasia in the Living Cell. Proc. Soc. Exper. Biol. and Med., 86:81, 1954.
88. Wegelius, O. and Hjelmaan, G.: Vital Staining of Mast Cells and Fibrocytes. Acta Path. Microbiol. Scand., 36:304, 1955.
89. Bunting, H. and White, R. F.: Histochemical Studies of Skin Wounds in Normal and in Scorbutic Guinea Pigs. Arch. Path., 49:590, 1950.

90. Jackson, S. F. and Smith, R. H.: Fibrous Proteins and Their Biological Significance. Symposia of the Society for Experimental Biology No. 9. New York, Academic Press, Inc., 1955.
91. Windrum, G. M.: Sulfation Technics in the Histologic Study of Granulation Tissue. Lab. Invest., 7:9, 1958.
92. Smith, R. H.: The Biosynthesis of Some Connective Tissue Components. In Butler, J.A.V. and Katz, B. Eds.: Progress in Biophysics and Biophysical Chemistry. New York, Pergamon Press, 1957, p. 218.
93. Jackson, S. F.: Fibrogenesis *in vivo* and *in vitro*. In Randall, J. T.: Nature and Structure of Collagen. New York, Academic Press, Inc., 1953, p. 140.
94. Stetten, M. R.: Some Aspects of the Metabolism of Hydroxyproline Studied with the Acid of Isotopic Nitrogen. J. Biol. Chem., 181:31, 1949.
95. Sinex, F. M. and Can Slyke, D. D.: The Role of Hydroxylysine in the Synthesis of Collagen., Fed. roc., 16:250, 1957.
96. Sinex, F. M. and Van Slyke, D. D.: The Source and State of the Hydroxylysine of Collagen. J. Biol. Chem., 216:245, 1955.
97. Stetten, M. R. and Schoenheimer, R.: The Metabolism of L (-) -Proline Studied with the Acid of Deuterium and Isotopic Nitrogen. J. Biol. Chem., 153:113, 1944.
98. Piez, K. A. and Likins, R. C.: The Conversion of Lysine to Hydroxylysine and its Relation to the Biosynthesis of Collagen in Several Tissues of the Rat. J. Biol. Chem., 229:101, 1957.
99. Smith, R. H. and Jackson, S. F.: Studies on the Biosynthesis of Collagen, II. The Conversion of 14C-L-Proline to 14C-Hydroxyproline by Fowl Osteoblasts in Tissue Culture. J. Biophys. Biochem. Cytol., 3:913, 1957.
100. Van Slyke, D. D. and Sinex, M. F.: The Course of Hydroxylation of Lysine to Form Hydroxylysine in Collagen. J. Biol. Chem., 232:797, 1958.
101. Dorfman, A.: The Effects of Adrenal Hormones on Connective Tissues. Ann. N. Y. Acad. Sci., 56: 623, 1953.
102. Meyer, K.: The Chemistry of Mesodermal Ground Substances. The Harvey Lectures, New York, Academic Press, Inc., 1957, p. 88.
103. Meyer, K.: The Chemistry of the Ground Substance of Connective Tissue. In Asboe-Hansen, G. Ed.: Connective Tissue in Health and Disease. p. 54, Copenhagen, Munksgaard, E., 1954.
104. Meyer, K., Hoffman, P. and Linger, A.: The Acid Mucopolysaccharides of Connective Tissue. In Tunbridge, R. E. Ed.: C.I.O.M.S. Connective Tissue. A Symposium. Springfield, Ill. C. C. Thomas, 1957, p. 86.
105. Consden, R.: Observations in the Composition of Human Subcutaneous Tissue. In Randall, J. T. Ed.: Nature and Structure of Collagen. New York, Academic Press, 1953, p. 196.
106. Dische, L., and Zelmenes, G.: Polysacchardies of the Vitreous Fibers. Arch. Ophthal., 54:528, 1955.
107: Dische, L., Danilczenko, A. and Zelmenes, G.: The Neutral Heteropolysaccharides in Connective Tissue. In Ciba Foundation Symposium on the Chemistry and Biology of Mucopolysaccharides. Boston, Little, Brown and Company, 1958, p. 116.
108. Glegg, R. E., Eidinger, D. and Leblond, C. P.: Presence of Carbohydrates Distinct from Acid Mucopolysaccharides in Connective Tissue. Science, 120:839, 1954.
109. Glegg, R. E., Eidinger, D. and Leblond, C. P.: Some Carbohydrate Components of Reticular Fibers. Science, 118:614, 1953.
110. Leblond, C. P., Glegg, R. E. and Eidinger, D.: Presence of Carbohydrates with Free 1, 2-Glycol Groups in Sites Stained by the Periodic Acid-Schiff Technique. J. Histochem. Cytochem., 5:445, 1957.
111. Pirie, A.: Composition of Ox Lens Capsules. Biochem. J., 48:368, 1951.
112. Schoenberg, M. D. and Moore, R. D.: Studies on Connective Tissue II. Histochemical Differences in the Connective Tissue Polysaccharides of the Mature and Immature Human Umbilical Cord. Arch. Path., 64:167, 1957.
113. Blumberg, B. S. and Ogston, A. G.: Further Evidence on the Protein Complexes of Some Hyaluronic Acids. Biochem. J., 68:183, 1957.
114. Blumberg, B.S. and Ogston, A. G.: The Effects of Proteolytic Enzymes on the Hyaluronic Acid Complex of Ox Synovial Fluid. Biochem. J., 66:342, 1957.
115. Ludwig, A. W. and Levin, S.: The Protein Fractions of Synovial Fluid and Umbilical Cord Mucins. J. Mt. Siani Hosp., 24:1017, 1957.
116. Blumberg, B. S. and Ogston, A. G.: Physiochemical Studies on Hyaluronic Acids. In Ciba Foundation Symposium on the Chemistry and Biology of Mucopolysaccharides. Boston, Little, Brown and Company., 1958, p. 22.
117. Shatton, J. and Schubert, M.: Isolation of Mucoprotein from Cartilage. J. Biol. Chem., 211:565, 1954.
118. Muir, H. M.: The Structure of a Chondroitin Sulphate Complex from Cartilage. In Tunbridge, R. E.: C.I.O.M.S. Connective Tissue. A Symposium. Springfield, Ill., C. C. Thomas, 1957, p. 294.
119. Partridge, S. M. and Davis, H. F.: The Chemistry of Connective Tissues. 4. The Presence of Non-Collagenous Protein in Cartilage. Biochem. J., 68: 298, 1958.
120. Mathews, M. B. and Lozaityte, I.: Sodium Chondroitin Sulphate-Protein Complexes of Cartilage. I. Molecular Weight and Shape., Arch. Biochem., Biophys., 74:158, 1958.
121. Neuberger, A.: Observations on the Presence and Metabolism of Plasma Proteins in Skin and Tendon. In Tunbridge, R. E.,: C.I.O.M.S. Connective Tissue. A Symposium. Springfield, Ill., C. C. Thomas, 1957, p. 35.
122. Sylven, B.: Uber das Vorkommen von Hochmolekularen Esterschwefelsauren im Granulationsgewebe und bei der Spithelialen Regeneration. Acta Chir. Scand. 86: Suppl. 66, 1, 1941.
123. Asboe-Hansen, G.: The Mast Cell. Intern Rev. Cytol., 3:399, 1954.
124. Grossfeld, H., Meyer, K., and Godman, G.: Differeniation of fibroblasts in Tissue Culture, as Determined by Mucopolysaccharide Production. Proc. Soc. Exper. Biol. and Med., 88:31, 1955.
125. Ludwig, A. W. and Boas, N. F.: The Effect of Testosterone on the Connective Tissue of the Comb of the Cockerel. Endocrinology, 46:291, 1950.
126. Riley, J. F. and West, G. B.: The Presence of Histamine in Tissue Mast Cells. J. Physiol., 120:528, 1953.
127. Wislocki, G. B., Bunting, H., Dempsey, E. W.: Metachromasia in Mammalian Tissues and its Relationship to Mucopolysaccharides. Am. J. Anat., 81:1, 1947.
128. Penny, J. R. and Balfour, B. M.: The Effect of Vitamin C on Mucopolysaccharide Production in Wound Healing, J. Path. Bact. 61:171, 1949.
129. Higginbotham, R. D. and Dougherty, T. F.: Mechanism of Heparin Protection Against a Histamine Releaser (48/80). Proc. Soc. Exper. Biol. and Med., 92:493, 1956.
130. Higginbotham, R. D.: Studies on the Functional Interrelationship of Fibroblasts and Ground Substance Mucopolysaccharides. Ann. N. Y. Acad. Sci. 73:186, 1958.
131. Curran, R. C.: The Elaboration of Mucopolysaccharides by Vascular Endothelium. J. Path. Bact., 74:347, 1957.
132. Boyd, E. S. and Newman, W. F.: The Surface Chemistry of Bone. V. The Ion Binding Properties of Cartilage. J. Biol. Chem., 193:243, 1951.
133. Kodicek, E. and Loewi, C.: Uptake of (35S) Sulfate by Mucopolysaccharides of Granulation Tissue. Proc. Roy. Soc., B., 144:100, 1955.
134. Gross, J., Highberger, J. H. and Schmitt, F. O.: Some Factors Involved in the Fibrogenesis of Collagen. Proc. Soc. Exper. Biol. and Med., 80:462, 1952.
135. Gross, J. The Behavior of Collagen Units as a Model in Morphogenesis. J. Biophys. Biochem. Cytol., Suppl., 2:261, 1956.
136. Meyer, K.: The Chemistry of the Ground Substances of Connective Tissue. In Asboe-Hansen, G. Ed.: Connective in Health and Disease. Copenhagen, E. Munksgaard, 1954, p. 54.

CONCEPTOS MODERNE IN RE LE TISSU CONJUNCTIVE

per Dr. chir. dent. e phil. George A. Krikos

SUMMARIO IN INTERLINGUA

Le facto que le cellulas del corpore es separate ab le circulation del sanguine per tissus conjunctive e que il es iste tissus conjunctive que assecura le transition de nutrientes ab le sanguine a in le cellulas e de productos metabolic ab le cellulas a in le circulation sublinea le importantia del tissus conjunctive in sanitate e in maladia.

Tissu conjunctive es componite de tres major elementos, i.e. le cellulas, le fibras, e le substantia basal. Differentias quantitative e qualitative in iste tres elementos resulta in le varietates de tissu conjunctive, como per exemplo le fibrose tissu conjunctive, le osso, le dentina, etc.

Es opinate que le fibroblasto, le osteoblasto, e le chondroblasto es active in le production de collageno e del mucopolysaccharidas in le substantia basal. Le factos currentemente disponibile suggere que le mentionate materiales es livrate per le cellulas in un forma precursori que alora es subjicite a alterationes in le spatios intercellular. Le natura del precursores que le cellulas livra remane ancora un thema pro speculationes.

Hodie, tres fractiones de collageno es recognoscite. Illos es (a) le fraction extrahibile per sal neutre, (b) le fraction extrahibile per citrato acide, e (c) un forma insolubile de collageno. Le secunde a le tertie pare esser de origine fibrillar, le prime de origine extrafibrillar.

Le substantia basal non es un substantia chimicamente uniforme sed es componite de un varietate de elementos de origine diverse. Le mucopolysaccharidas acide ha essite studiate le plus extensemente, sed il pare que le plus grande proportion del polysaccharidas in tissu conjunctive es libere de acido uronic. Le componentes del substantia basal ha un rolo importante in le ligation de aqua, le distribution e thesaurisation de cationes extra-cellular, le mechanismos de distoxification, le determination del proprietates de fibras de collageno, e possibilemente le fibrillogenese.

Le cellulas, le fibras, e le substantia basal del tissus conjunctive es tres intimemente interrelationate e interdependente elementos.

THE EFFECT OF PRESCALING UPON HEALING FOLLOWING PERIODONTAL SURGERY — A CLINICAL AND HISTOLOGIC STUDY*

IRVING GLICKMAN, B.S., D.M.D.†

The impression has been created in periodontal circles that good clinical practice requires that teeth should be scaled before periodontal surgery is performed. This preliminary scaling is referred to as "pre-scaling." It has been claimed that by reducing the inflammation in the periodontal pocket wall, prescaling "conditions" the tissues and thereby improves the healing and reduces the healing time following periodontal surgery.[1, 2] Because of the interest on the part of clinicians in the question of prescaling it was felt a service would be rendered by exploring the validity of the aforementioned claim. A correlated clinical and histologic study was therefore conducted in humans to determine the effects of pre-scaling upon healing following periodontal surgery.

EXPERIMENTAL PROCEDURE

The experiment was designed so that one side of the mouth was pre-scaled, and one was not. Gingivectomy was performed two weeks later on the pre-scaled side and the non-pre-scaled side. Healing of the two sides was compared at one, two and four week intervals following the gingivectomy. The total duration of the experimental period was six weeks. At all stages of the experiment, clinical observations were accompanied by biopsies of the gingiva. Ten patients were studied. They were treated by different operators. The "pre-scaling" consisted of the removal of supra and subgingival calculus. The experimental procedure employed for each patient is outlined in the following chart.

CHART I

RIGHT SIDE

1. Photo before treatment comparing both sides
2. Pocket measurement—both sides
3. Biopsy before scaling
4. Scaling and return for Oral Physiotherapy
5. Photo, one week post-scaling—Comparing both sides
6. Photo—two weeks post-scaling—comparing both sides
7. Biopsy two weeks post-scaling
9. Gingivectomy—2 weeks post-scaling
11. Photo one week post-gingivectomy—comparing both sides
12. Photo two weeks post-gingivectomy—comparing both sides
13. Biopsy two weeks post-gingivectomy
15. Clinical picture four weeks post-gingivectomy—comparing both sides
16. Biopsy four weeks post-gingivectomy

LEFT SIDE

8. Biopsy before gingivectomy
10. Gingivectomy
14. Biopsy two weeks post-gingivectomy
17. Biopsy four weeks post-gingivectomy

OBSERVATIONS

Clinical examination and biopsies indicated the presence of periodontal pockets with inflammation and degeneration of the gingiva on both sides of the mouth at the outset of the experiment (Figs. 1 & 2). Pre-scaling resulted in reduction in the severity of gingival inflammation in the two-week period before gingivectomy was performed.

There was clinical and microscopic evidence of progressive healing at the one week, two week, and four week post gingivectomy intervals. The rate of healing varied from patient to patient. In individual patients, there were no significant clinical (Figs. 3 & 4) or microscopic differences (Figs. 5 & 6) in the post-gingivectomy healing of the pre-scaled and non-prescaled sides.

* From the Ziskin Memorial Research Laboratory, Department of Periodontology, Tufts University School of Dental Medicine, Boston, Mass.

† Research Professor of Oral Pathology; Professor and Chairman of the Department of Periodontology.

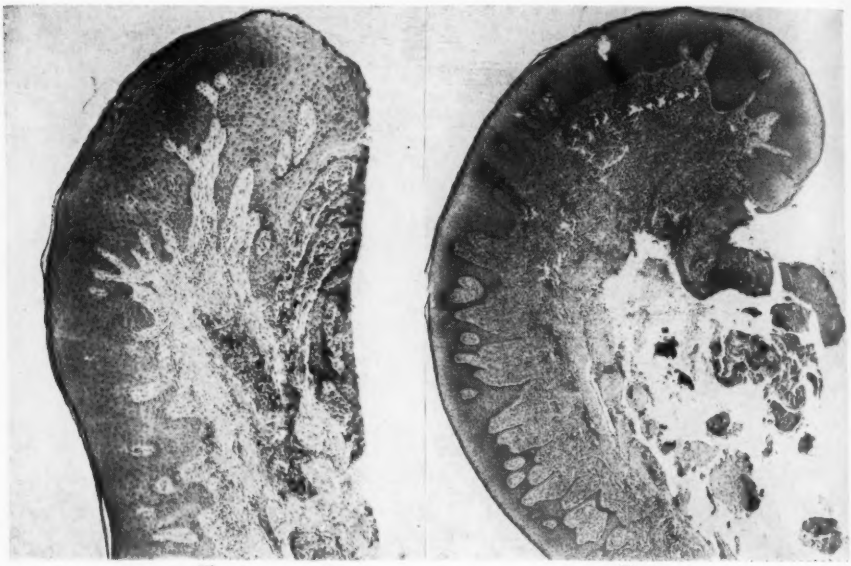

Fig. 1 Fig. 2

Fig. 1. Inflammed periodontal pocket wall before pre-scaling. Hematoxylin and Eosin orig. mag. X 50.

Fig. 2. Inflammed periodontal pocket wall on side which was not pre-scaled. Hematoxylin and Eosin orig. mag. X 50.

Fig. 3. *Top Left.* Before treatment. The right side was pre-scaled two weeks before gingivectomy. Gingivectomy was performed on the left side without pre-scaling. *Top Right.* One week after gingivectomy. *Bottom Right.* Four weeks following gingivectomy—pre-scaled side. *Bottom Left.* Four weeks following gingivectomy—non-pre-scaled side. (Patient of Dr. Thomas O'Brien)

Fig. 4. *Top.* Before treatment. *Center.* Immediately following pack removal after gingivectomy. Right side was pre-scaled. Left side was not. *Bottom.* Comparable appearance of healed gingiva on pre-scaled and non-pre-scaled sides. (Patient of Dr. Carlos Mendoza)

DISCUSSION

Our results are similar to those of Ambrose and Detamore[3] who, in a comparable study, could find no conclusive evidence of a beneficial effect of pre-scaling upon healing following periodontal surgery.

It was not the purpose of this investigation to promulgate a directive as to whether teeth should or should not be pre-scaled prior to periodontal surgery. This remains largely a

Fig. 5

Fig. 6

Fig. 5. Four weeks post-gingivectomy on the side which was pre-scaled. The gingival margin has been restored, the epithelium is well formed, and the connective tissue is densely collagenous. There is inflammatory infiltration at the base of the sulcus. Hematoxylin and Eosin orig. mag. X 50.
Fig. 6. Four weeks post-gingivectomy on the side which was not pre-scaled. The appearance of the tissue is comparable to that on the side which was pre-scaled. Compare with Fig. 5. Hematoxylin and Eosin orig. mag. X 50.

matter of individual preference. There are many who pre-scale because they feel that after the inflammation of the periodontal pocket wall has been reduced, there is less bleeding when the surgery is performed and they can operate more efficiently. On the other hand there are others who perform surgical periodontal procedures without pre-scaling who do not find bleeding to be a problem.

It was the purpose of this investigation to attempt to determine whether pre-scaling exerts a conditioning effect upon the tissues and thereby improves the healing and reduces the healing time. Our findings indicate that pre-scaling exerts no such beneficial effects.

CONCLUSION

In a correlated clinical and histologic study performed in ten human subjects the findings indicated that "pre-scaling" did not improve the healing or reduce the healing time following periodontal surgery.

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BIBLIOGRAPHY

1. Orban, B.: "Periodontics; a Concept-Theory and Practice," C. V. Mosby Co., St. Louis, 1958, p. 174.
2. Glickman, I., Goldman, H. M., Thomas, B. O. A., and Ramfjord, S.: "Is Scaling Prior to Gingivectomy a Necessary Procedure," J. Western Society Periodontology, 4:99, 1956.
3. Ambrose, J. A., and Detamore, R. J.: "Correlation of Histologic and Clinical Findings in Periodontal Treatment," J. Periodont., 31:238, 1960.

LE EFFECTO DEL PRE-DISCRUSTAGE SUPER LE REPARO DEL TRAUMA DE CHIRURGIA PERIODONTAL — UN STUDIO CLINIC E HISTOLOGIC

Dr. med. dent. Irving Glickman (B.S.)

SUMMARIO IN INTERLINGUA

In un correlationate studio clinic e histologic in dece subjectos human, le constatationes indicava que "pre-discrustage" non meliorava le reparo o reduceva le tempore de reparo de trauma per chirurgia periodontal.

Le resultatos del presente studio es simile a illos de Ambrose e Detamore[3]. In un studio de character comparabile iste autores trovava nulle nette indication de un effecto benefic del pre-discrustage super le reparo de trauma per chirurgia periodontal.

Le objectivo del presente studio non esseva promulgar directivas con respecto a si o non le dentes debe esser discrustate in preparation a chirurgia periodontal. Le responsa a iste question remane in alte grado un cosa de preferentia subjective. Multes effectua pre-discrustage proque illes opina que post que le inflammation del parietes periodontal es reducite, le operation evoca un minus forte sanguination e pote esser executate plus efficacemente. Del altere latere, il etiam es multes qui effectua interventiones chirurgic periodontal sin pre-discrustage e qui non trova que sanguination constitue un problema.

Le objectivo del presente studio esseva determinar si o non le pre-discrustage exerce un effecto super le tissu e meliora assi le reparo e reduce le tempore del reparo. Nostre constatationes indica que le pre-discrustage non exerce ulle tal effecto benefic.

EMOTIONAL FACTORS IN CHRONIC DISEASES*

FRANZ ALEXANDER, M.D.†

In recent years there is a growing interest among physicians in the influence of emotional factors upon organic diseases. This interest is not entirely novel; in a sense it is older than the organic orientation in medicine. The medicine man of the pre-scientific era tried by ritualistic performances to exorcise from the body of the patient the evil spirit which took hold of him and made him sick. We do not need, however, to go back to our prehistoric past. Modern physicians were for long aware of the influence of the patient's psychological condition upon the course of his disease. They even attributed etiological significance to emotional factors in producing organic symptoms, as is well demonstrated by expressions in use even today, such as "gastric or cardiac neurosis," or the older expression—"asthma nervosa."

What is new in the current preoccupation with psychological factors in disease is the attempt to describe the elusive emotional factors more precisely and understand their influence upon body functions in scientific terms.

This new orientation became known under the term "psychosomatic medicine".

It is now generally recognized that in studying the totality of organic processes, both psychological and physiological methods are required. Stomach secretion as an isolated process in itself can be studied only by the methods of biochemistry; its nervous control, however, cannot be studied completely by physiological methods alone because the latter cannot adequately account for certain central (emotional) influences without utilizing psychological information. For example, the fact that receptive dependent wishes mobilize stomach secretion cannot be ascertained by physiological approach because these wishes cannot be identified by any existing physiological method. Theoretically, emotional influences can be studied also as brain processes; practically, however, this will be possible only after physiological techniques have been developed by which different emotions can be identified. The question whether or not in this hypothetical future state of medical knowledge, the psychological approach will be substituted by brain physiological techniques, is an open one.

I do not want at this time to go into the philosophical discussion of the age-old body-mind problem. In my address I shall deal with observations and theories which are independent of what position one takes concerning the body-mind problem. My own position corresponds to a statement which we published in 1943 when we organized the *American Journal for Psychosomatic Medicine:* "We take for granted that psychic and somatic phenomena take place in the same biological system and are probably two aspects of the same process, that psychological phenomena should be studied in their psychological causality with intrinsically psychological methods and physiologic phenomena in their physical causality with the methods of physics and chemistry."

Noticing that nostalgic feelings stimulate gastric secretion, we study the psychological stimulus in terms of psychology, its physiological end-effects with physiological methods. We do so because the neurophysiological correlary of nostalgic feelings at present cannot be identified; nostalgia itself cannot be studied by any other but psychological techniques. Specific emotional tensions activate different physiological functions; for example, rage, as Cannon's experiments have shown, stimulates a host of physiological processes, such as carbohydrate metabolism and circulation, leading to elevation of blood pressure.

Such basic observations stimulated the psychoanalytic study of patients suffering from

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† Director, Psychiatric and Psychosomatic Research Institute Mount Sinai Hospital, Clinical Professor of Psychiatry, University of Southern California, Los Angeles, California.

various chronic organic conditions. Emotional patterns characeristic for certain diseases have been described as a result of extensive and detailed psychoanalytic observations.

GENERAL DYNAMIC FORMULA

The general dynamic formula is that whenever certain impulses become repressed or inhibited in their adequate expression in interpersonal relations, a chronic, emotional tension state develops, which because of its chronic nature exerts a continued influence upon certain vegetative functions. Although the intermediary physiological mechanisms are still largely unknown, the interaction between the initiating psychological tension state is well established. A chronic frustration of the wish to receive help and love, which due to neurotic conflict situations cannot be satisfied in interpersonal relations, stimulates the stomach functions which, if it persists over a longer period in predisposed individuals, may lead to ulcerations in the duodenum. Here too, the intermediary physiological chain of events is not fully known. That the psychological tension state, a receptive longing for help, however, activates stomach secretions is well established.

I should like to repeat here an important consideration, which I have made in previous writings, namely, that such specific psychophysiological correlations, no matter how well established they may be, do not offer a final etiological explanation of chronic diseases in which emotional factors have been described. The knowledge of such correlations merely accounts for the role of the emotional factor, but not for complete etiology. The same emotional conflicts can be observed in persons who do not suffer from any organic symptoms. In order to explain the organic condition, other predisposing factors, to which we may refer with the expression, "specific organ vulnerability", must be postulated. This vulnerability may be either constitutional—transmitted by genes—or acquired early in life by child-rearing practices or by previous diseases involving the organ system in question. The familial nature of many of these chronic diseases is indicative of the constitutional component. Early diseases in the history of some patients involving the organs, which later become affected by emotional tension states, again indicate acquired vulnerability of organ systems.

Only the two types of factors together, organic predisposition and specific emotional tension-states, can account for the observations made in patients suffering from those chronic diseases which have been hitherto studied by the psychosomatic approach.

EMOTIONAL FACTORS IN DIFFERENT CHRONIC DISEASES

There is a rapidly growing knowledge about the emotional factors which are characteristic for different chronic diseases. In the last 25 years in the Institute for Psychoanalysis in Chicago, we have been engaged in the study of patients suffering from different chronic conditions such as hypertension, peptic ulcer, asthma, neurodermatitis, arthritis, colitis and thyrotoxicosis. Our studies convinced us that the psychological picture in these diseases is highly specific. The specificity pertains to the emotional conflict pattern but not to the emotional components of the conflict. Sexual impulses, aggressive feelings, dependent needs, anxiety and guilt, curiosity and the wish for love and security are common to all human beings and are found equally in normal and diseased persons. What we found specific is the psychodynamic interrelationship between these psychological elements. This finding has its counterpart in organic chemistry where the great diversity of organ compounds contains the same four basic elements—carbon, oxygen, nitrogen and hydrogen. Their chemical property differs depending upon their stereochemical configuration, whether the hydrogen atom is directly attached to the carbon ring or through an oxygen atom, makes a difference in the chemical properties of the two compounds. Psychodynamic patterns also contain the same elements but in different structures. For example, hostility may be the result of frustration of dependent longings. If a person is extremely dependent upon love and acceptance by others, he is apt to repress his hostile feelings. This pattern is different from one in which the person reacts to his dependent

tendencies with shame, and in order to remedy this shame engages overtly in aggressive and hostile behavior. These simple examples may illustrate what is meant by psychodynamic patterns.

In our clinical studies of the last 25 years we have succeeded in formulating seven different patterns, each characteristic of one of the seven previously mentioned conditions. These patterns appeared with great regularity and yet we felt the need to test the validity of findings by more reliable techniques. Psychoanalytic formulations are made on biographical material as remembered by the patient and are characterized by an abundance of detailed data interrelated with each other in an infinite complexity. In many respects, this type of material resembles historical material on which histographers base their reconstruction and explanation of historical events. Both historical and psychoanalytic material are characterized by an abundance of details which are connected in multiple ways and like ink blot tests they allow the perception of a great variety of partial patterns. It is theoretically assumed that all these partial patterns form a total gestalt—a kind of master pattern. The perception of this total dynamic gestalt in an unequivocal way is never possible and the most ingenious observers can at best propose a theory of high plausibility. In the historical sciences, including psychoanalysis, validity of a reconstruction has been based on internal consistency. This brings about the type of persuasion which is called plausibility. Internal consistency and plausibility are, however, not equivalent with validity. Validation requires the verification of certain consequences of a formulation by independent data, which are not included in the formulation itself. This may consist in predicting a future event or a current event unknown to those who made the formulation.

The most desirable method of validation is to predict unknown facts which are established by other independent techniques. Psychosomatic studies are of such nature. The interconnectedness of psychological and physiological processes allows us to establish an event in the organism by two different and independent techniques: physiologic and anatomic on the one hand, and psychological on the other hand. If it is true, as we found in our clinical studies, that a certain psychological pattern always be possible to diagnose the organic condition from the presence of the psychodynamic patterns alone. If "A" always appears in connection with "B", the knowledge of "B" can serve to conclude the presence of "A". The presence of a duodenal ulcer can be established by x-ray, hypertension by sphygmographic methods. If they can be also diagnosed independently by psychodynamic formulations, this would validate the postulated correlation between the organic disease in question and a certain specific psychodynamic pattern.

VALIDATION PROCEDURE

In the last five years we have undertaken in Chicago such a validation procedure. One member of a team of psychoanalysts interviews a patient belonging to one of the seven diseases described above. This interview is duly mechanically recorded in its entirety. From the transcribed record the interviewer eliminates all data pertaining to the patient's organic disease. This material is further censored by a medical reader. This doubly-edited record is then submitted to the other members of the team. This version contains nothing but biographical and psychological data. The task of the team is to diagnose the patient's disease on the basis of this expurgated material which contains only psychological data. The same material is also submitted to a group of medical practitioners, internists, who have no knowledge of the psychodynamic constellations which are the basis of the diagnosis of the psychoanalytical group. This is our control Group. The results of both groups are then compared and statistically evaluated. Two conditions must be fulfilled in order to validate the correctness of the psychosomatic correlations: (1) the psychoanalytic group should be able to diagnose exclusively from psychological data the disease more frequently than chance probability. Since we know that the patient in each case suffers from one of the seven diseases, the probability of making the correct diagnosis without any

theory merely by chance is once in seven times. (2) The medical group, provided that the medical clues are successfully eliminated from the records, should not be able to do much better than expected by chance and significantly less frequently than the psychoanalytic team.

Our study is still in process, but our preliminary results indicate that these two requirements are being fulfilled. On the average, we are able to diagnose correctly the patients in 56 per cent of the cases. The final data concerning the performance of the control group is not yet available.

After some preliminary remarks, I shall try now to give a thumbnail sketch of the psychological patterns which in our psychosomatic studies we found characteristic in the seven chronic diseases I mentioned before. In traces all the seven patterns may appear in one and the same person. It is possible, however, to identify either the central conflict, or those defenses which have psychosomatic implications.

We used in our studies two operational concepts: the first is the psychodynamic constellation, the central confiict, together with the defenses employed against it; the second is the onset situation. The latter, too, is a psychological concept. It refers to the psychodynamic situation in which the patient found himself just before his first symptoms developed. The onset situation is defined as the external life situation as it affects the patient. The same external life situation may have different meaning for different persons. For example, being left by his wife may mean a great loss for one patient and a relief for another. We refer, therefore, with the term "onset situation" to life conditions immediately preceding the illness as they affect the patient emotionally at that time.

In general terms our findings can be reduced to the following statement: A patient with a characteristic psychodynamic constellation develops a disease when the turn of events in his life are suited to mobilize either his central conflict or break down one of his primary defenses. In other words, with some luck, if the right external situation never occurs, a patient, in spite of the presence of the predisposing emotional patterns, may never develop the disease.

As mentioned before, this statement requires, however, a most important qualification. In addition to the characteristic psychodynamic constellation and the corresponding onset situation, we postulate a third category of etiological factors, the "X" factors, which consist in the vulnerability of the affected organ. This somatic predisposing factor we cannot identify at present, and yet feel compelled to assume its presence. This "X" factor we assume has a complex multiple determination such as heredity, early organic diseases affecting an organ system, and possibly also early physiological habits. The disease is a result of the coexistence of these three categories of factors —the organic "X" factor consisting in a specific organ vulnerability, the typical psychodynamic constellation and the onset situation. These three factors together are responsible for the disease.

EXISTENCE OF "X" FACTOR

As previously stated, we had to postulate the existence of the "X" factor because the same psychological factors— the psychodynamic patterns and the corresponding onset situation— may be present in patients who never develop the organic disease. For example, there are many persons who have the type of defense against their hostile impulses as found typically in essential hypertensives, who never develop hypertension even if the external life situation is suited to mobilize their aggressive impulses, and prohibits their free expression. Only those persons who have in addition to these psychological factors a constitutional vulnerability of their vascular system respond with hypertension. The significance of the psychological factors, on the other hand, we had to assume because we found them present in all cases we subjected to careful scrutiny. Moreover, the psychological factor, precisely the central confiict, we find operative before the onset of the disease, reaching far back in the patient's early history.

These three variables, constitution, psychological patterns formed in early life, and the precipitating life situation are not necessarily independent variables. It is quite thinkable that constitution—at least partially determines both the organ vulnerability and the psychological patterns. At present we know little about the interdependence of the two variables. There is strong indication, however, that the correlation between constitution and characteristic pattern is not a simple one. Constitution alone without certain emotional experiences of early life may not produce a consistent pattern. We are particularly impressed by the significance of the early mother-child relationship which is determined not only by the hereditary equipment of the child, but also by the psychological characteristics of the mother.

Neither do we consider the onset situation as an entirely independent variable. It is not purely a chance factor. Patients with certain psychological predisposition may unconsciously seek out certain life situations to which they are sensitized. For example, hypertensives, as will be developed later, are characterized by the tendency to carry on dutifully their work even under difficult and harrassing conditions. Such a person who carries a load without externally revolting against it is more apt to get into life situations in which he is exploited by his environment. Such a "beast of burden" type of patient is likely to be loaded down by heavier and heavier weights just because he so patiently submits to indignities.

After these preliminary remarks I shall turn now to the description of the patterns characteristic for these seven diseases we have studied in the last 25 years.

DUODENAL ULCER

In patients suffering from peptic ulcer the central dynamic factor is the frustration of dependent desires which originally were oral in character. The craving to be fed later appears as a wish to be loved, to be given support, money and advice. This finding originally made in the Chicago Institute for Psychoanalysis since has been corroborated by a number of other authors. This strong fixation to the early dependent situation of infancy comes in conflict with the adult ego and results in hurt pride since this infantile craving for help is contrary to standards of the adult to his wish for independence and self-assertion. Because of this conflict it must be repressed. As a rule, the frustration of oral dependent cravings leads to oral aggressive impulses. The psychodynamic formula is: If I do not receive what I want I must go out and take it by force. Oral receptiveness thus changes into oral aggressiveness. This acquisitive impulse may also become repressed because of the guilt feelings which it provokes. We see then that both the oral dependent and the oral aggressive impulses may be frustrated by internal factors.

The most common defense against both oral dependent and acquisitive impluses is overcompensation. These latently dependent or acquisitive persons overtly become independent hard-working individuals who like responsibility, take care of others, and respond to challenges with increased active strivings. The go-getter businessman who never relaxes is a common example. In a sense, these persons live beyond their emotional needs. The harder they work and the greater responsibilities they carry on their shoulders, the greater becomes their internal secret need to lean on others. These repressed dependent cravings because they are excluded from overt gratification sustain a persistent emotional tension. Receiving food is the first gratification of dependent needs and it becomes the prototype for all help-seeking wishes. To be loved, to be helped, is associated from the beginning of life with the wish to be fed; when this help-seeking attitude is denied from normal manifestation in a give-and-take relationship to others, a psychological regression takes place to original form of the wish to incorporate food. This desire seems to be specifically correlated with increased gastric secretion.

Not all patients suffering from duodenal ulcer overcompensate for their dependent desires with an outward show of go-getting activity and acceptance of leadership and responsibilities. Many of them are overtly dependent, demanding and disgruntled. In such persons

the dependent tendencies are frustrated not by internal repudiation but by external circumstances. But even those patients who are frustrated by external circumstances, and seek help overtly, show a definite conflict about their helplessness. The crucial factor in the pathogenesis of ulcer is the frustration of dependent help-seeking and love-demanding desires. When these desires cannot find gratification in normal human give-and-take relationships, a chronic emotional stimulus is created which has a specific effect on the functions of the stomach.

Onset occurs when the intensity of the patient's unsatisfied dependent cravings increases either because of deprivation or because the patient defends himself against his unconscious help-seeking tendencies by assuming increased responsibilities. External deprivation often results from the loss of a person on whom the patient was dependent, or from leaving home, or the loss of money or position, which had given the patient a sense of security. The increased responsibility may result from getting married, a new child is added to the family, or from accepting a new and more responsible job.

ULCERATIVE COLITIS

The central dynamic factor in these patients is losing hope to be able to accomplish a job involving responsibility, effort and concentration. These patients are inclined to give up easily in the face of obstacles; even though they may continue their efforts toward achievement internally, they already have lost their confidence and have given up their hopes. In the past history of these patients we find often that already in early childhood they were exposed to challenges which were beyond their capacity, and had seductive mothers who impatiently pushed their little child toward becoming a man. The parents of these patients have as a rule great expectations toward their child's performance and transplant their own ambition for achievement into the child. The relative weakness of the patient's ego to achieve the goal which is set higher than their capacity often leads to a disintegrating process of paranoid coloring which explains the frequent combination of psychotic symptoms with ulcerative colitis.

The physiological mechanism is far from being clearly established in these cases. My own view is that we deal here with a regressive psychodynamic process: a regression from meeting the challenges of life on a mature level to a more primitive form of accomplishment on the gastrointestinal level. Defecation is one of the first accomplishments of the child for which he receives praise from mother. Increased intestinal activity in the form of evacuation becomes an infantile substitute for coordinated efforts on the adult level.

The mechanism is not fully understood through which the urge toward accomplishment should increase peristaltic activity. The last phase of evacuation, however, is under voluntary control and it is by no means impossible that the activity of the colon can be stimulated through the ano-colic reflex—innervations ascending from the anal sphincters toward the colon, possibly even to the small bowel. From the point of view of etiology it is important to note that clinical evidence indicates that the role of psychogenic stimuli may consist merely in favoring an independently existing local organic disease process.

BRONCHIAL ASTHMA

The central conflict in these cases stems from internal impulses which threaten a person's attachment to mother or a mother substitute. Some mothers react to the first signs of the little child's sexual strivings directed toward them with withdrawal or rejection. Sexual strivings thus become an internal danger threatening to alienate mother's affection. Later in life a very common precipitating situation leading to asthma attacks is a pending marriage which these patients are apt to procrastinate. Long periods of engagement have been observed in a number of patients. The son senses the mother's disapproval of his planned marriage and is caught between his love for his bride and the fear of losing mother's love. The girl, too, may sense mother's unconscious jealousy and is torn between her sexual desires

and fear of maternal disapproval.

A further specific feature of these patients is their conflict about crying. Crying is the child's first device for calling mother. In these patients crying is inhibited because of fear of maternal repudiation. Inability to cry is a common finding in asthmatics. Asthmatic patients' mothers show an ambivalent attiude—seductive and rejecting at the same time. Later in life the difficulty of calling mother by crying gives place to a difficulty in confiding in an unpredictable mother. These patients have a conflict between their wish to confide and the fear of it. Thus, the fear of alienating mother becomes centered on verbal communication which explains the involvement of the respiratory function. Asthmatic attacks can be understood as an inhibition of utilizing the expiratory act for communication, either by crying or confession.

ESSENTIAL HYPERTENSION

In these cases a continuous struggle against expressing hostile aggressive feelings and the patient's difficulty in asserting himself in any fashion are the central issue. These patients fear losing affection of others and therefore they control the expression of their hostility. Yet, as children they were prone to have rage attacks and be aggressive. Sometimes rather suddenly, sometimes gradually, a change in personality occurred. The formerly aggressive child, prone to temper tantrums, changes to a person who cannot assert himself and is overly compliant. The experience of losing the parents' and other people's affections by aggressive behavior induced them to control their hostile impulses.

Another related trend is their dogged perseverance in pursuing even insuperable obstacles. Their life history is often that of the beast of burden. They frequently have long-standing job records, staying with the same company even when underpaid for many years. If they are promoted to executive positions, they encounter difficulties because of their inability to assert themselves and to make others follow orders. Their inclination is to do the job of others instead of insisting on discipline.

The continued control of their own self-assertive and aggressive impulses creates a tension state, which, though still not fully established neural and endocrinological channels, contributes to the chronic elevation of blood pressure. The fact that they were prone to carry an excessive load of work and responsibility, even without adequate recompensation, increases their resentment, which in turn necessitates greater and greater control of these hostile feelings. A vicious circle develops, leading to a chronic tension state.

The characteristic onset situation consists in life circumstances which mobilize hostility and the urge for self-assertion, and at the same time prohibit their free expression. The characteristic job situation is where a person is required of greater accomplishment without rest or salary, and at the same time is threatened with losing his job, if he would show the least sign of his discontent or rebellion.

NEURODERMATITIS

In these cases we find a complex configuration between exhibitionism, guilt and masochism, combined with a deep-seated desire to receive physical expression of love from others. In the history we find, as a rule, undemonstrative mothers who create in the child a great hunger for that type of stimulation of the skin which goes with the physical expression of love on the part of the mother toward the child. They want to be stroked, to be cuddled. In general, close physical contact is what is lacking, something which was never sufficiently satisfied in their early life. They try to get attention by the means of infantile exhibitionism, which is apt to induce the adults to cuddle the child.

The early exhibitionist techniques of getting attention and love are aimed at winning the one parent's attention away from the other parent. If successful, these may become connected with guilt. The guilt manifests itself in these patients in a characteristic trend to put their wrong foot forward, to appear in a bad light, to make embarrassing faux pas, to make fools of themselves.

It is impressive to observe how often in the history of these patients we find physical punishments, whipping and beating. The body

surface, particularly the skin, becomes highly charged by emotional cathexis. The skin is the site of exhibitionism in both a positive and negative sense and also the site of pain. The sexual impulses in these patients in which skin eroticism is accentuated become deeply linked with guilt feelings. Pleasure mixed with pain is their solution. They pay with pain for their guilt laden exhibitionistic successes.

The disease, as a rule, is precipitated after the patient achieves some form of exhibitionistic victory. The victory arouses guilt and creates a need for suffering precisely on that part of the body which is involved in the exhibitionistic success. By scratching, which is a substitute for masturbation, the patient relieves both sexual tension and at the same time inflicts pain upon himself. Some patients vividly describe the pleasure which they derive from scratching. They refer to it as a vicious kind of pleasure. In these scratching orgies they attack their body mercilessly. They experience scratching as a pleasureful pain or a painful pleasure. The most general precipitating circumstance, however, is the wish for loving human contact after being separated from persons to whom they are attached.

RHEUMATOID ARTHRITIS

Like the hypertensive patients, these patients also have great difficulty in handling their aggressive hostile impulses. Unlike hypertensive patients, however, their solution is a combination of self control and benevolent tyranny over others.

Most of our knowledge is derived from arthritic women patients. (Arthritis is 7 times more common in women than in men.) When they become mothers they show compulsive trends and have the inclination to control all the moves of their children and demand their participation in the daily chores of the household. Interestingly in their own childhood they were exposed to similar maternal influences. The typical mother of the arthritic patient is a restrictive one. In their history we hear consistently the story that as children they were mostly punished by the deprivation of their physical freedom. "Stay put" is the characteristic command of the mother of the arthritic patient. As young girls in the pre-puberty period they react to this physical restriction by becoming tomboys, competing with the boys, fighting with them, climbing trees and fences. This muscular activity is highly eroticized. In this way they drain the pent up rebellion against maternal restrictions. Later in life the tomboy's physical expression of rebellion becomes transformed into the tendency to tyrannize others. This they can do without guilt because they exert a helpful type of tyranny. They are strict but take care of the interests of their underlings.

The arthritic condition develops often when this drainage of hostile impulses, by helping and ruling at the same time, is blocked by some change in their external life situations. Loss of persons whom they dominated before is one common precipitating condition. Arthritic women usually marry submissive men and wear the pants in the family. Repeatedly I have seen the precipitation of the disease when the husband made a valiant and successful attempt to stand up against the domination of the wife.

In other cases, the interruption in some kind of physical outlet is the precipitating factor leading to increased tension. The psycho-physiological processes through which these emotional factors influence the disease process are largely unknown. There is, however, good indication that increased muscle tonus, that is to say, increased simultaneous innervation of both flexors and extensors, may be a factor which unfavorably influences the arthritis process. Most probably this is not a primary etiological factor, but increased muscle tonus seems to have a detrimental influence upon the course of the disease, which has other somatic sources. This may explain the capricious nature of the disease characterized by the unpredicatable sequences of relapses and remissions.

THYROTOXICOSIS

The central dynamic issue is a constant struggle against fear, unadulterated biological fear concerning the physical integrity of the body and even more specifically, fear of death. What is characteristic, however, is the way these patients handle their fear. They try to

master it by denying it and in coping with the dangerous situation rely only on themselves. In their history we find regularly frequent exposures to death of near relatives and other traumatic events which constituted a threat to survival. Equally characteristic is the fact that they mature rapidly. A six-year-old motherless girl who cooked for the whole family and was the little mother to her younger siblings is a typical example.

The denial of fear leads to a counterphobic attitude, to the tendency to seek out actively just those situations which they are afraid of and repressing the fear of them. The precipitating situation is often some kind of threat to survival in which the counterphobic defense breaks down. Thyrotoxicosis following immediately a traumatic event, such as accidents, became known under the term "Shock-Basedow". In other cases only careful methodical scrutiny can reveal the threatening event immediately preceding the outbreak of the disease.

The psychophysiological explanation of the close correlation between fear and thyroid dysfunction is still not complete. The fact that these patients have the tendency for early maturation and to meet dangers in a self-sufficient way may well account for a constant stimulation of thyroid function which, after all, consists in the acceleration of growth and metabolism in general. Also the relation of thyroid function to anxiety is well established, a relation which goes both ways. Anxiety activates thyroid function and thyroid hyperactivity manifests itself in increased alertness, vigilance, and fearfulness.

The onset situation may be sudden trauma. This type of etiology has been long known and found expression in the term "Shock-Basedow". Sudden physical trauma, however, will produce thyrotoxicosis only in predisposed individuals—predisposed not only by heredity and constitution but also by the type of a life history in which threat for mere survival repeatedly occurred.

These psychodynamic correlations found in these seven diseases have by now largely been substantiated by the type of validation studies which I briefly described. I want to call attention to the fact that these psychophysiological correlations make physiological sense. In ulcer patients it makes physiological sense that dependent, help-seeking tendencies should have a specific correlation to stomach activity, the connecting link being the association between the wish to be loved and the wish to be fed.

It makes physiological sense that in asthma patients we find the inhibition of the urge to communicate with others. The first communication of the child with the mother is through crying. The asthma attack consists in inhibition of the expiratory phase of the respiratory function—which is involved in crying.

It makes physiological sense that patients who develop thyrotoxicosis show an early tendency toward maturation and for long-term planning. Thyroxine is an accelerator of metabolism and of the whole maturational process. Thyroxine increases alertness and is called upon when the organism faces long-term effort. In pregnancy, for example, the thyroid gland normally increases in size.

It makes physiological sense that the arthritic process is unfavorably influenced by increased muscle tonus which results from the simultaneous mobilization of aggressive impulses and their inhibition—a kind of strait-jacket situation.

It also makes physiological sense that the psychogenic factors in neurodermatitis are connected with both exhibitionistic tendencies and with the frustrated desire for physical contact as an expression of intimacy and love, a kind of contact-hunger. Blushing clearly demonstrates the involvement of the skin in exhibitionism. The blushing person in spite of himself betrays his hidden feelings.

It is only in colitis in which the psychophysiological correlation found in our studies has no easily explainable physiological meaning. That the frustrated urge for accomplishment should lead to increased motility of the bowel can be, however, explained if we remember the fact that one of the earliest accomplishments and prides of the infant derives from the excremental act.

Our studies demonstrate that the above described organic diseases are not only characterized by certain pathophysiological processes, but they have at the same time their own psycho-

pathology. Particularly significant is the fact that the psychopathological process involved in these diseases seems to have a definite etiological significance.

I do not want to leave this subject without emphasizing the therapeutic implications of these findings. The knowledge of specific psychosomatic correlations in different chronic diseases makes a more goal-directed and active therapeutic approach possible in the comprehensive treatment of the patient. The general medical management must be coordinated with psychotherapy.

In all the above discussed chronic diseases the somatic management alone seldom can bring about permanent remedy. The somatic treatment of the damaged or vulnerable organs is only half of the therapeutic task. The chronic emotional stimuli resulting from emotional conflicts which affect the diseased organ system must also be eliminated or reduced to insure a permanent cure.

FACTORES EMOTIONAL IN MORBOS CHRONIC

per Dr. med. Franz Alexander

SUMMARIO IN INTERLINGUA

Recente annos ha vidite un marcate augmento del interesse de medicos pro le influentia de factores emotional super le morbos organic. Iste interesse, in un certe senso, non es nove; in un certe senso illo es plus ancian que le orientation organic del medicina. Le magos del era prescientific tentava per practicas ritualista exorcisar ab le corpore del patiente le spiritos malefic que habeva invadite le e que rendeva le malade. Sed il non es necessari retraciar nostre passos usque a nostre passato prehistoric. In nostre tempores, le medicos ha semper recognoscite le influentia que le condition psychologic del patiente exerce super le curso de su morbo. De facto, illes attribueva un signification etiologic a factores emotional in le production de symptomas organic, un facto que es ben demonstrate per expressiones que nos usa currentemente, como per exemplo "neurose gastric" o "neurose cardiac," o que esseva usate non longemente retro, como per exemplo "asthma nervose."

Le nove elemento in nostre currente preoccupation con le factores psychologic in le phenomenos pathologic es le desiro de describer ille elusive factores emotional plus detaliatemente e comprender lor effecto in le functiones del organismo de maniera precisemente scientific.

Le clarification de specific correlationes psychosomatic sub le conditiones de diverse morbos chronic permitte un plus consciemente orientate e un plus active attitude therapeutic in le tractamento global del patiente. Le programma general del therapia medical—isto es nostre objectivo —debe esser coordinate con principios del psychotherapia.

In omne le morbos chronic que es discutite in le presente articulo, le tractamento exclusivemente somatic es rarmente capace a effectuar un curation. Le tractamento somatic del organos vulnerate o traumatisate es solmente le prime medietate del labor therapeutic. Il es etiam necessari eliminar le chronic stimulos emotional que resulta ab conflictos emotional, i.e. conflictos que affice le suffrente systema organic. Il es solmente le elimination de ille stimulos, o al minus lor reduction, que pote assecurar un curation durative.

THE UNSOLVED PROBLEM OF DENTAL CARIES

JACOB YARDENI, D.D.S.*

The etiology and mechanism of dental caries still pose many perplexing questions in spite of its great prevalence and the constant search for a solution of this problem. The more we study the problem, the broader its aspects seem to be. As one dips into the vast literature on caries, one finds, to one's great dismay and confusion, that the whole field is controversial, and that the many conflicting data have given rise to a considerable number of conflicting theories, old and more recent. To quote Nuckolls[1]: "At the present time, there exist many different hypotheses as to the etiology and pathogenesis of caries", and he lists 15 theories. We may be permitted to add a few more[2, 3, 4, 5].

THE MONISTIC THEORIES

The argument begins with the consideration of the dual composition of the tooth structure, organic and inorganic. This calls for a dual mechanism of action, and is reflected in the two main rival theories of demineralization and proteolysis. The controversy continues as a red thread along every aspect of caries research: role of sugar, susceptibility and resistance, specific bacteria, salivary protection, the nature of erosion, mode of fluor action, and prevention in general. Figure I illustrates a few controversial issues listed at random on which divergent opinions are current:

FIGURE I

The caries process starts by:

1. Demineralization (chalky enamel) caused by:
   a. Acids (pH 4.5) b. Chelation (pH nearly neutral)
2. Bacterial invasion and yellow pigmentation of:
   a. Enamel b. Dentin

Substrate:

a. Keratin or other organic substance b. Collagen c. Mucopolysaccharides[6, 23].

Main organisms involved:
Lactobacilli, Actinomycetes, Streptococci.

THE ACID THEORY (1890)

One of the earlier concepts, the so-called chemicoparasitic theory, was announced by W. D. Miller[7] some seventy years ago, and in time it became recognized as the classical theory on caries. Judged by its broadly conceived title, which includes both chemistry and bacteria, it could be adapted with equal success to polarly opposed theories, such as proteolysis, chelation and others. Its actual meaning, however, is much narrower. The full comprehension of its meaning can be elucidated from Miller's own interpretation: "Microorganisms do not exert a direct influence on enamel. Their action on the enamel in the first stage of decay is therefore indirect, that is they act by means of the acid which they produce through fermentation of refined carbohydrates."

The title was only a frame which had to be filled in by future spadework. It is based on evidence of experiments *in vitro,* the well-known Miller's triad: cut teeth were placed in a mixture of saliva and bread at a temperature of 37°, and in three months the dentin was softened. However, the biological environment of a functioning tooth was missing. Acid formed by fermentation is self-limiting and acts upon the surface, whereas actual caries is three-dimensional, and is characterized by a conical penetration, with the apex reaching the dentin. Bacteria in initial caries are usually found within the enamel, before a visible lesion has developed,[18, 19, 59] and the organic constituents of the enamel play a great part in controlling the shape and progress of the lesion.[8] Thus, Miller only charted the overall course of its process, but there has been a too

* Lecturer, School of Dentistry, Department of Anatomy, Hebrew University-Hadassah Medical School, Jerusalem, Israel.

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Leave Bermuda	— Monday,	May 29 —	12 Noon
Arrive Nassau	— Wed.,	May 31 —	9 AM
Leave Nassau	— Wed.,	May 31 —	6 PM
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"RECENT TRENDS IN DENTAL MEDICINE"

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J. Lewis Blass, Ph. G., D.D.S., "Gaining Acceptance for Specialty Dentistry."

Milton Hyman, D.D.S., "A Simple Clinical Approach to the Treatment of Temporomandibular Joint Dysfunction."

Symposium on Dental Medicine—Section Participation

Harry Roth, B.S., D.D.S., Moderator
"Desquamative Gingivitis"

William M. Greenhut, B.S., D.D.S.
"Diabetes"

Leslie Milne, D.M.D.
"Pemphagus"

Martin R. Protell, B.S., D.D.S.
"The Hypochondriac Patient"

Earl Stone, D.M.D.
"Atypical Haemophilia"

Dr. Rudolph W. Palermo
111 Larch Drive
New Hyde Park, L.I., N.Y.

Dear Dr. Palermo:

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.....

literal interpretation of his theory which, as such, already has a long tradition, almost from biblical times. Still, it has continued its victorious march for decades, since it was comforting to have a theory able to explain, even if only in a general way, at least the main features of the disease. Thus, the dogma of acid prevailed, and with it the confusion on the major issues of this universal disease of civilized mankind.

A cross section through the current theories is given in a recent symposium on oral bacteriology[9]. Homage is first paid to the authority of Miller: "The accumulated evidence supports Miller's conclusion that decalcification of enamel by acid is the initial and crucial step of the carious process". A few lines further we read: "Microbial destruction of the organic matrix might be the first step in caries". And on the next page, an alternative mechanism gains importance: "On the other hand, decalcification might be accomplished near neutrality by chelation, i.e., the formation of stable heterocyclic complexes, such as calcium forms with citrate." It is known, in fact, that acid is not the sole factor causing decalcification, and that chelation reagents are potential solvents of the minerals of enamel, even under alkaline conditions.[10, 11]

THE REAL PROBLEM

Carious research is still beset with many problems. Foremost of all, the acid theory failed in its most avowed purpose: in the field of clinical appreciation and caries prevention. "One billion unfilled cavities" is indeed a sad state of affairs, and one may readily share Bagnall's just complaint: "It is difficult to understand the single-minded concentration of so many workers during the first half of this century"[12]. At the same time, while we are still struggling with the problem of caries, rickets has almost completely disappeared. This contradicts the view, still held by some, that rickets is of singular significance in the etiology of dental caries[13].

Now, a theory of a disease is said to be strong if it is built on four pillars: etiology, mechanism, pathogenesis and prevention. A study of the newer literature is not very encouraging in any of these respects.

And yet there is no doubt that acid may exert a deleterious action on the enamel as a whole, not on the mineral component alone, since at a certain low pH it may affect the organic structure as well and cause its swelling. In fact, swelling may take place at both sides of the isoelectric point, since enamel possesses amphoteric properties[20]. Swelling is a potent biophysical factor, sufficient to make the tooth structure more readily available for bacterial invasion. According to Scott et al[18], "If demineralization does precede damage to the enamel matrix, however, the openings in the meshwork of submicroscopic fibrils within and between the prisms are much too small to accommodate bacteria. These spaces would have to be enlarged by some means, chemical or physical, before bacterial penetration could be effected". Swelling may be the mechanism in action. It is a common effect of acid action on the organic matrix[16], manifested histologically by the characteristic widening of the tubules at the expense of the surrounding matrix, and by the interstitial striae which appear thickened and swollen.

Mandel[28] postulates some mechanical disruption of organic material and attributes it to carbon dioxide formed in the process of decalcification. According to Westin[25]: "The prisms of the enamel have lost their mineral content, as seen from his fig. 30, which shows the cavern walls *distended by internal pressure*" (italics ours). B. Gottlieb[24] reports that the organic framework seen in carious lesions is far thicker than it would be if it were merely the organic framework freed from mineral salts." The degradation of the proteins into smaller units is accompanied by increased osmotic pressure causing imbibition. This swelling is an accompanying physical phenomenon, readily affecting proteins in the process of demineralization, since with the removal of the calcium ions, which electrically bind the calcium-protein macromolecule, repelling forces take over, the framework loosens, gets imbibed and swollen. The pathways for bacterial invasion become widely open, and the organic matrix becomes accessible to lysis by oral bacterial enzymes.

ENAMEL "VITALITY" OR MATURATION DYNAMICS

For decades, enamel was considered an inert and practically dead tissue, fixed for a lifetime. The organic stroma, which amounts to about 2, 5% by weight, has been disregarded and it was maintained that demineralization alone could account for the loss of enamel. Modern scientific tools, at the electron-microscope level, give a different picture of enamel, as made up of delicate fibrils which form a reticular ground substance, that permeates the substance both within and between the enamel rod[30]. This picture must bear a greater relation to the truth than drawn before.

Clinically, the "inert" enamel of younger subjects reacts with a peculiar sensation of pain when biting on sour fruits. Conversely, later on, even erosion of the vestibular cervical enamel is hardly manifested by any subjective sensation. This is due to a gradual recession of the pulp and deposition of secondary dentin. We must thus admit a physical and physiological transmission of a stimulus from the enamel to the pulp, probably due to diffusion.

Miller[7] asserts that decalcification alone of enamel probably signifies its total destruction. Similarly, a recent theory (1957) maintains that caries is an electro-chemical dissolution of a dead structure.[5] Today, however, we are witnessing an era of complete rehabilitation of enamel. "This structure, once 'proven' to be purely inorganic, has now been shown to carry on an exchange of its substance with the body fluids. For instance, ions of phosphorus and iodine can penetrate through the enamel in both directions"[31]. "The incorporation of phosphorus into all regions of enamel and dentin was not merely a passive process, but in order to occur at its maximum the tooth has to be vital"[32]. The protoplasmatic extensions of the odontoblasts are in organic connection with the tufts, prism sheaths and lamellae, and may serve as essential channels for fluid exchange.[33]

"Using Miller's methods", says Sognnaes[34], "his observations can be repeated and have been confirmed extensively. But his interpretations and the sufficiency of his tools can now be questioned. In brief, it has become increasingly apparent that Miller's concept of enamel was in part derived from artifacts"[34].

Human teeth, which in fairy tales are likened to ivory castles, show in fact surface irregularities, perikymata, rod ends, cracks and scratches[36, 37]. A "smooth tooth surface" is a verbal fiction, it virtually does not exist. In our experiments (to be published), intact extracted teeth were washed, scrubbed, rinsed and blotted dry. They were then immersed in alcohol for two minutes and flamed. This procedure was repeated twice. Following this, the teeth were incubated for 48 hours. In most of the cases the broth appeared turbid. Bacteria were probably nested in the surface irregularities, or they emerged from within the organic channels.

Enamel presents to the clinican almost no problems other than mechanical, as long as we deal with routine preparations of cavities. But problems arise the moment we care to consider more fundamental issues of pathogenesis and etiology. It is only the gross morphology of the teeth which is fixed at an early developmental stage. There are particularly pertinent clinical observations and experimental data demonstrating that the period after teeth erupt is one of importance in the overall life history of the teeth[38]. Juvenile teeth, "fresh" from their crypts, are "poor risks" in certain operative procedures, before protective dentin has formed, or before enamel has maturated.

The seemingly "dead" enamel is undoubtedly a factor in the process of caries resistance. Phenomena such as bilateral caries, the age curve of caries incidence, and variable susceptibility of vital teeth may serve to illustrate this point.

There are a few recent data available on the subject of posteruptive changes, which are chemical, physical, functional and gerodontical.[18, 51] They involve problems of permeability and "vitality". "Microscopic study of predetermined areas of gingival, middle and occlusal thirds of enamel surfaces showed a consistent increase in the amount and intensity of surface pigmentation with increasing age".[39]

In general, there is a parallel between reduced permeability of tooth structure with age

and reduced caries incidence. This speaks rather in favour of the decisive importance of the organic matrix in the pathogenesis of caries. Cases of arrested caries are more frequently met with in older subjects: "Aged collagen has an increased capacity for binding calcium".[50] According to Hall[22], "At least half of the organic material in the fibers which are present in young enamel are replaced by inorganic material as it becomes more mature".

Beust[41] too has suggested that "sclerosis" of enamel and dentin is part of the mechanism of caries resistance.

Volker, et al.[40] report that "If hamster molars are exposed to high sugar diets immediately upon eruption, they are most susceptible to severe tooth decay." If contact with sugar is delayed until after the tooth surface has an opportunity to mature, the molars are most resistant to decay."

Early functional maturation consists in decrease of the water content and increase in specific gravity (gr/ccm).[42,43,44]

Frisbie, et al.[45] assume that the changes which occur in developing enamel continue after eruption, the process of progressive dehydration or desiccation, eventually giving a protein which is more resistant to hydrolysis. Teeth become more compact and less permeable, viz. less susceptible to caries. Mineral ions of the saliva in contact with the tooth surface probably contribute to this secondary calcification.[23, 46, 47] Adequate function results in accelerated maturation, and should therefore be considered a physiological factor of acquired resistance. And yet, teeth without antagonists are not any more caries-susceptible, as should be expected according to the "disuse" theory. What is the mechanism of decay? That is the pivotal problem, the solution of which holds the key of prevention.

Susceptible areas vary with advancing age: juvenile "pre-caries" areas and senile caries have different localizations.[52] Black's classification of cavities closely parallels the age sequence of affected areas, from fissure-to cervical caries. There is evidence to the fact that superficial enamel gradualy incorporates more fluorine than the rest of it.[48] But according to H. H. Neumann, while fluorides reduce decay at a ratio of "1 to 2", "natural" diets are effective at a ratio of 100 per cent, and this even with fluoride-free waters. "Look at the footsoles of some barefoot walking natives, and see what the pressure does to the hardness of the keratin. The ground substance of the enamel is a keratin too". (Personal communication).

We may thus assume, that if our teeth have been successfully carried over through the maturation period in young age, they are likely to remain resistant for the coming years. The surface irregularities are eliminated with time by functional attrition which is accelerated by proper use and functional mechanics. The slogan "see your dentist once a year" may well apply to older patients; school children should be advised to check their dentition at much shorter intervals. In some individuals, teeth do not mature for some yet unknown reason, and such "juvenile" teeth need constant vigilance. "We may be dealing with enamel in a matrix state in many incipient carious lesions." [49] It should be noted, however, that spaced teeth are less subject to decay, irrespective of age, of functional use or physical properties of food one consumes, but simply because all tooth surfaces are self-cleansing. This may be one of the main factors of freedom from caries of teeth of carnivora. If there is no food retention, no "enrichment medium" on which bacteria can thrive, there will be no caries. The experiment with tube feeding is a convincing illustration of such an ideal arrangement.

Conversely, following radiation therapy and ensuing xerostomia, even hitherto resistant teeth fall prey to a peculiar, often circular type of rampant caries. Teeth and saliva are one functional system, and if salivary protection is at fault, the teeth deteriorate. The picture of dissolution of tooth structure is unique. We would not even call it caries; at least, it is very atypical.

Concerning the permeability of the organic pathways, Applebaum remarks that "it is not a very simple matter, since it involves the

question of membrane charge and porewall phenomena". In his experiments with dyes, an unerupted tooth was used, because teeth become denser after eruption". According to Atkinson,[54] the difference between young and old enamel is in the outer layer only. It may well be assumed that the surface becomes better crystallized as a result of "work hardening" and of salivary precipitation. It follows that investigations *in vitro* regarding permeability or susceptibility of intact enamel should be carried out on newly erupted teeth only.

In summing up we should say that demineralization as evidenced by clinical radiography, is an undisputable feature of dental caries, and that sticky carbohydrates are the main cariogenic factors. Combined with permeability they encompass the entire problem of pathogenicity of enamel caries.

THE PROTEOLYTIC CONCEPTION: PRO AND CON

a) Mechanism

Histologic evidence first heralded by C. Bodecker[55] to the effect that enamel is essentially organic constitutes a turning point in caries research. Corroborated by later evidence, with the aid of histochemistry and radioisotopes, it eventually led to the re-examination of the fundamental concept of the caries process. Indeed, it represented a radical change from the ingrained view of the inertness of enamel to one of a defensive reaction, passive or active. It became clear that the organic substance is involved in the process and may even be the site of the primary attack. According to Ross, 50% of the cavities commence in fissures and grooves. "It is significantly interesting", says Ross[56], "that in these areas the groove protein and the cuticle remain, for the brush bristles are too thick, in comparison with the groove diameter. It is likely that in these areas the initial attack is a proteolytic one. These areas are filled with organic debris, desquamated epithelial cells and keratin from the slow receding epithelium: an admirable framework for bacterial growth."

With regard to smooth surface cavities, "it has been shown that in a clinically caries-free tooth a lesion can be produced in the dentin by microorganisms which invade and pass down an enamel lamella. This is true proteolysis" [57]. Several other investigators[58] have pointed to organic pathways as gates for bacterial invasion, thus proferring an antithesis to the prevailing theory of acid decalcification. The enamel keratin is not a chemically homogenous entity, nor is the collagen of the dentin. Sognnaes and Wislocki[6], using histochemical methods concluded that caries is initiated by demineralisation and depolymerisation of the mucopolysaccharides* normally present in the interprismatic substance and in the dentin. Once the acid-soluble mucopolysaccharides have been broken down, the collagen fibers become susceptible to lysis by a number of organisms.[16]

Similarly, Pincus[73], Stack and Sullivan[14] have reported the presence of a soluble mucoprotein in normal enamel. Sullivan's sections of lesions stained by the periodic acid-Schiff method revealed a change between the prisms, "the earliest sign of any change in the enamel, which the author was able to detect" [14].

Bacteriological studies *in vitro* of Hurst[59] et al. "incline the authors towards the hypothesis that enamel penetration and caries initiation may occur either independently of, or simultaneously with, acid decalcification". "There results, though not entirely conclusive, are compatible with the hypothesis that utilization of the organic matter may be a factor in caries" (Ibide 6: 1454, 1953). This hypothesis was not sustained by the tube-feeding experiment. Would bacteria be able to utilize the organic structure, caries would undoubtedly have developed, for there was no lack of bacteria in the oral cavities of the hamsters in this experiment.

b) Clinical appearance

The profound difference in conception makes itself manifest even in such statements as related to the external appearance of the early

* Mucopolysaccharides have a low protein content and are predominantly carbohydrate. Any substance which acts chemically on the mucopolysaccharides, will alter the physical nature of the ground-substance and affect its permeability.

carious lesion, perceptible by simple visual examination. According to Miller[7], "as the first indication that the process of destruction has begun on the external surface of the enamel, we notice that it has lost its normal polish and transparency; then a white irregular spot of chalky color appears." Normal enamel reflects the light and it appears shining. Decalcified enamel causes diffusion of light rays, which impart to the enamel a chalky appearance. But chalky enamel can be smoothed and polished. It may disappear by subsequent recalcification or it may become brownish which would indicate caries.[27]

Brown discoloration, in complete contrast to the presumed white appearance of the initial carious attack, has been observed by many more investigators. In fact, it is a difference in essence, not in appearance alone, for it is a question of acid action or proteolysis. As a matter of fact, brown discoloration is often superimposed on a chalky spot, particularly on approximal surfaces.

"The earliest and simplest form of lesion associated with slow caries may be seen clinically as a darkly stained area without any breach in the enamel surface."[57] "The Kodachrome shows a more advanced stage of dentin involvement, with the characteristic yellowish-orange pigmentation. The evidence as determined by the grenz-ray criterion of no decalcification or negligible decalcification of lesions, which by histologic examination are revealed as enamel caries, leads to the conclusion that acid formation is not a necessary precursor of enamel caries".[61]

According to Evans and Prophet,[63] "proteolysis and decalcification, both occur at pH 6.0-6.8, and to be effective in causing caries they must at least act simultaneously". The proteolytic-chelation theory is based on just such an assumption.[4,64]

B. Gottlieb, a histologist of great distinction, was only one of the representatives of the "new conception" [65]. True, histology can give indirect clues only, but some substantiation of his concept came from other quarters, such as physiology, histochemistry, radioactive isotope research, and others.[14, 66, 67, 68]

"Studies with polarized light on the birefringence of enamel indicated that caries most nearly resembles a process in which there is initially a preferential loss of organic matter." [69]

With regard to the clinical appearance, there is a marked lack of uniformity in the terminology used in describing the various changes in enamel caries[81]. There are "white spots" [3] and brown spots[65] and "inner spots" [87] and "closed lesions" [66]. Which of them is of particular significance in initial caries? And is it really a matter of semantics alone? According to Kronfeld[90], a "white" spot is a very early stage of superficial decalcification of enamel. "This condition can hardly be called caries." In a recent paper[60] we read: "The first clinical manifestation of dental caries is the development of white regions in the enamel." But, as it often happens with clinical evidence, which does not lend itself to dogmatic generalizations, we find a different description a few pages further: "The observations of prisms

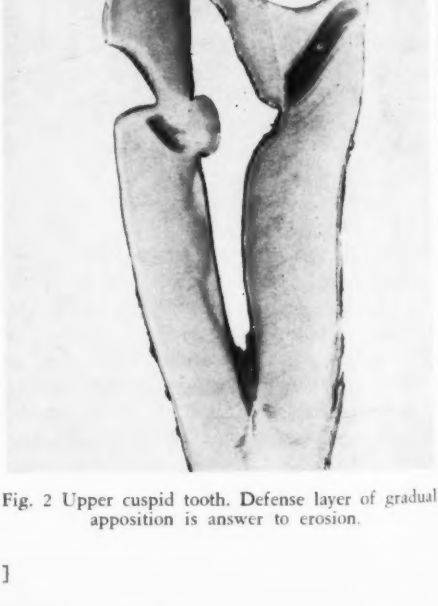


Fig. 2 Upper cuspid tooth. Defense layer of gradual apposition is answer to erosion.

protruding from the surface of the brown spot in fig. 28, without any visible support, suggest loss of interprismatic substance rather than pronounced decalcification and weakening of the prisms." (Compare our Fig. 2.)

However, the cardinal question of what makes sound organic structure liable to invasion or decomposition remained without answer. "The organic matrix of intact, untreated dentin does not react readily with diazohydroxide, neither is it readily accessible for lysis by ordinary proteolytic enzymes." [71] No oral bacteria were so far found able to attack enamel keratin; neither is dentin accessible to proteolysis, since no collagenase has been known to occur in the oral cavity.

Gottlieb[65] has postulated that the cuticle, lamellae, interrod substance, rod sheaths and tufts are potential avenues of bacterial invasion and the sites of a primary attack. In fact, it would make the problem simpler if we should differentiate between these two aspects: a) pathways of penetration, and b) mode of attack. It can be said that it is widely agreed that specific pathways of penetration are those mentioned by Gottlieb, be it for acids, dyes, radioactive isotopes, enzymes or bacteria. There is no agreement, however, with regard to the mode of attack. Is it primarily one of demineralization, or of proteolysis or both simultaneously? Even the nature of alteration of the organic substance is not established unequivocally.

Gottlieb was honest with himself. One day he told me, that something had been disturbing him all the time, but that now he believed that he had worked it out. Unfortunately, he died soon afterwards. The studies on proteolysis are, however, unlikely to slacken quickly, and in fact they have been resumed with new vigour by a group of competent bacteriologists[4,64]. Whereas the evidence for decalcification is rather spectacular and is supported by methods both simple and direct, proteolytic studies are more subtle, more complicated, rather presumptive, and therefore not always unequivocal. They are forthcoming in bits and pieces, for they require elaborate histochemical methods and modern tools. No wonder that "bacteriological evidence supporting the proteolytic conception is limited".[62] (One can hardly contradict this statement of Bartels'). There are cases of youngsters complaining of an offensive breath. Upon examination, it appears that their mouth flora is essentially proteolytic, yet their teeth are excellent.

In the "historical" perspective of 15 years, we readily agree now that Gottlieb's conception was premature enough. In his lack of knowledge of the chelation mechanism at an alkaline pH, he became entangled in a lot of contradictions, for it was not easy to do away with the evident signs of decalcifications* and he became hopelessly confused with the "acid producers". He was forced, therefore, into a difficult position of defence, and the entire conception remained for a while more mental than experimental.

Very recently, however, valid statistical and biochemical data in support of Gottlieb's conception and of the efficiency of his prophylactic method were supplied by Gurkan of Istanbul,[72] and Scharpenak of Moscow[21]. Such experiments need repetition by competent workers.

PROTEOLYSIS-CHELATION: A NEW THEORY OF DENTAL CARIES

Of late, a remarkable series of investigations was reported by a group of scientists, headed by Dr. Albert Schatz. The concept resulting from the integration of proteolysis and chelation, is, in part, a re-evaluation of the largely reported proteolytic theory in terms of modern biochemistry. It explains the etiology of dental caries as two interrelated reactions of one overall mechanism, decalcification and proteolysis, occurring simultaneously.[4]

This conception has enriched the fundamental mechanism of the carious process by the new premise of chelation (Greek: chele—claw), a chemical reaction that can remove calcium from the calcium-proteinate complex of enamel or dentin at a nearly neutral pH. In fact, several workers before, among them McClure and Ruzicka,[10] Pincus,[73] Nikiforuk

* which he wrongly interpreted as signs of acid action exclusively.

and Sreebny[11] reported chemical disintegration of the crystalline structure of the enamel at a high pH, which is inconsistent with the classical view for acid decalcification. Forscher and Fosdick,[74] mention the tendency of sugar to complex with calcium ions (instead of fermentation). Investigations of Ockerse and Jager[88] point to the assumption that in the velvet monkey caries may develop in an alkaline environment. Chelation seems to be the logical explanation of such observations. The followers of the proteolytic theory may be right in asserting that caries begins and ends with the organic structure. Ignore it, and one is dealing with inert dead structure, in which no disease is conceivable. Demineralization is not specific, but caries is certainly specific, even caries of enamel. One should only bear in mind the composite histopathology of the early carious lesion.[81]

"An appreciation of the abundance of the chelates which come in contact with the enamel can be gained from consideration of some of the better known naturally occurring chelates. they include amino-acids, hydroxy—and keto—esters, carboxylates, fermentation products and others. They also occur in food, saliva and plaque material and are among the products of microbial activity."[75]

Peptides and amino-acids are chelating agents. It means that the degradation of the organic matrix leads to formation of chelates *in situ,* within the enamel or dentin. Methods of paper chromatography proved the presence in carious dentin of aspartic and glutamic acids, both a result of breakdown of the protein matrix by bacterial enzymes and, both relatively strong chelators, capable of demineralization of enamel and dentin *in situ*.[68] Thus, a vicious cycle is created: the chelates draw the calcium which is mainly responsible for holding the calcium-protein complex in a closed ring by electrostatic and coordinative links. With the removal of the positively charged calcium, and of the soluble mucoproteins, the macromolecule is loosened, and the road for bacterial invasion is opened. Proteolysis takes place, and new chelates are formed.

According to this so-called proteolysis-chelation theory, decalcification and proteolysis are not necessarily mutually exclusive, since both may take place at a neutral or alkaline pH. Chelation supplies the missing link between decalcification and proteolysis. In fact, one of the chelates—citrate—is well known for its affinity to calcium, and it is indicated as the cause of the cervical erosion.[10] However, in this case chelation is dissociated from proteolysis, and caries fails to occur. This fact still lacks explanation.

"The main difference between demineralization by chelation or by acids consists in the more pronounced and deeper dissolution of the interprismatic substance than of prism rods by the chelator."[76] Our experiments with Versen appear to confirm this observation (Fig. 2).

This is in agreement with a previous observation by Keil, who compared the optical behaviour of caries enamel and etched enamel. According to Keil, acid destroys prisms, whereas initial caries destroys the interprismatic substance. Shaw and Gupta[77] question, however, the nature of the effect of chelators, because of "the lack of any striking influence of EDTA supplementation on occlusal caries." But generally speaking, it appears that the criterion of a caries-potentiating agent should be its effect on the smooth surface and not the occlusal sulci, since the "precarious" fissures which usually become infected shortly after eruption[59] may obscure the issue and may make the evaluation complicated. The very histology of the fissure is different: there is more organic substance in it[78] and more numerous pathways for bacterial invasion, to start with. Therefore, we may not go very much wrong, if we agree to judge our experimental results by enamel changes on the smooth surfaces, and leave the occlusal pits and fissures alone. McClure,[79] Zipkin and McClure,[89] Coolidge and Jacobs[26] used smooth surface caries as a model of their studies.

Still unsettled is the old controversy originally raised by Miller whether bacteria invade in advance of alteration, or alteration precedes invasion. The proteolytic-chelation concept contends that both events are interdependent and

proceed simultaneously. It conforms to the conception of Orland[86] who believes that "dental caries is in all probability a convergent biological phenomenon, in which there must be the coincidental occurrence of at least three conditions: a microbic flora, a nutrutive substance and suboptimal resistance." Likewise, Appleton is of the opinion that "factors in caries do not form a "causal chain," but a complicated 4-dimensional network."[85] We may add that the fourth dimension is the factor of time, since the necessity and availability of all the factors for the caries process to begin makes its course slow.

The proteolytic-chelation theory seems to be "tailored" to conform to such a network, for it is self-perpetuating and keeps the process going in a "vicious cycle." The onset of caries is slow, because heterogenic reactions (solid-liquid) take longer.

However, some criticism on the role of chelation in caries initiation should be mentioned. The red lake formed by alyzarine red S in initial caries speaks for liberation and redeposition of free calcium from the calcium protein complex and points to acid action. In chelation, as known, the soluble calcium complexes are transported away, and equilibrium is shifted to one side. Besides, amino-acids formed *in situ* are weak chelators of calcium, having a log constant of 1.5 v. 10.5 of synthetic EDTA (Versen). Even citrates which have a stronger affinity for calcium, have a log constant stability of 3.2 only. This may mean "hanging heavy weights to slender wires," although citrates are believed to be related to the most intriguing phenomenon of cervical erosion. Why is there chelation with no proteolysis, although cervical enamel contains at least fifty per cent more organic fibers than the cuspal enamel.[22] In contrast with undermining caries, erosion is an open lesion, with a wide open frontier of a potential attack. It starts in the cervical enamel and deepens gradually as if being carved out. It facilitates stagnation and retention of debris, yet caries respects this wedge-shaped defect and keeps "out of bounds." What determines this phenomenal resistance in one mouth, whereas in another one cervical caries prevails? What is wrong with the neatly knitted "network"? Any general theory on caries ought to be able to account for such striking discrepancy. In the opinion of Schatz, "what appears to be most needed for further understanding erosion as well as caries and certain other oral conditions is a kind of detailed "biochemical geography" of the mouth."[29]

The only conclusion so far is that there is a natural biological equilibrium between attacking forces and defence reactions. The thick wall of protective dentine undoubtedly speaks of active resistance (Fig. 3); the lack of anaerobiosis, i.e. its very openess is another kind of a safety valve, and the differential oral microflora may be the most decisive factor.

THE BASIC PATTERN OF ENAMEL CARIES: ZONES OF CARIES

The initial carious lesion reveals several alternate layers of hypo-and hypercalcified enamel. Burnett and Scherp,[71] and Darling[2] differentiate four such layers. The different zones or layers of the initial lesion of enamel caries are clearly shown by polarized light, manifesting changes of a chemical nature. Scott and Albright[18] differentiate three zones: a zone of advanced destruction, an intermediate zone of "altered enamel," and an inner zone of apparently normal enamel. In a more de-

Fig. 3 Buccal surface of a lower deciduous second molar treated by the window method of Brudevold.[17] Kept in Versen pH 7.0 for 13 hours. Grinded after embedding in methyl methacrylate. The affected enamel is "mapped" in clearly defined microscopical structure.

tailed study on "The histopathology of caries of human dental enamel," Gustafson[81] demonstrated the presence of five distinct zones in initial caries identical on smooth surfaces and in fissures. These are, from within outwards:

1) A zone of increased mineralization
2) A zone of mineral solution
3) A zone of recalcification
4) A zone in which mineral solution was accompanied by destruction of the organic matrix.
5) A zone of complete destruction.

Zones four and five are practically identical, and zones one and three are recurrent. Anyhow, more detailed investigations have revealed an underlying complexity in what was for decades considered uniquely simple. However, although the various zones are of particular interest as an important guidepost to the specific factors involved in the caries process, they are unfortunately still in need of an unequivocal interpretation. According to Applebaum,[53] "In initial caries, the superficial layer maintains a marked X-ray absorption, even though the subsequent zones are partially decalcified and become more permeable to X-rays." This hypercalcified surface layer is originally present in normal enamel, as is revealed by chemical analysis, exchange experiments with radio-calcium and other methods. X-ray examinations done by Thewlis[83] suggest that there is a highly calcifled layer of enamel, about 0.1 mm thick, which invests the subsequent layers of enamel, like a skin. It is of interest that such findings inspired several investigators to proclaim that caries originates within the tooth (Siegmund, Jarmer),[84] or is due to an infarct of the "ultra-capillaries of the enamel" (De Vries).[3]

II. The subsurface of radiolucent enamel, as seen by grenz-ray or X-ray examination, is a phenomenon of decalcification hitherto regarded as indisputable evidence of acid action. But it is definitely not necessarily so, since decalcification is equally achieved by chelation, and, it is time we put an end to the confusing interchange of such terms as decalcification and acid.

III. The Mummery layer is a zone of hypercalcification, in contrast with the layer of hypocalcified enamel. Similarly, carious dentin shows an analogous transparent layer due to sclerosed tubuli, with the lumina obliterated. The Mummery layer is attributed to precipitation of free calcium ions from the adjacent layer of dissolution. The rhythmic succession of acid and alkaline zone in the immediate vicinity seems to determine their precipitation. This transparent layer may serve as a good argument to prove acid action. On the other hand, chelation of a high order of stability would signify mobilisation of tooth minerals and formation of soluble non-ionic complexes removed by salivation, hence the calcium ions may no longer be available for precipitation. This point needs further clarification.

The dentino-enamel junction and its relation to the carious process is of particular interest. Some deny the existence of a membranous structure and believe it to be an artifact or an optical interface. Losee et al.[35] used polarization, fluorescence, microradiography, and ultraviolet absorption techniques for the study of the structure of this region. The presence of a hypermineralized zone of 20-30 micron depth could be demonstrated by each of the four modes of investigation, as well as a broad zone of hypomineralization superficial to it. Their findings suggest that the lateral spread of the caries at the DEJ may be due to one or both of the following mechanisms:

1. "The process is confronted with a barrier at the DEJ, and considerable time is required to penetrate it and pass through to the dentin.

2. The process breaks into a natural channel along the DEJ, in which it finds little resistance to its progress compared to continuation in its initial direction. The concept that both may serve as mechanisms simultaneously suggests that a series of layers or zones of different compositions occupy the junction space."

MORE QUESTIONS TO BE ANSWERED

According to Shaw[32] animal experiments offer "a tremendous opportunity to find out why the teeth of these animals have such vastly different abilities to withstand the oral en-

vironment to which they are subjected. Is it a matter tooth composition or of tooth form? Is their saliva of strikingly different composition? The answers are unknown. Somewhere in the constitutional difference between these two strains lies a very important answer to one of the world's most prevalent diseases."

Experiments *in vitro* are still more undecisive: Thus, a report on a recent caries study in the artificial mouth is preceded by the following generalisation: "With the rather general concept of the carious process as an external attack by microorganisms, the process seems almost ideal for *in vitro* studies"[80] The author's conclusion, however, is quite different: "It cannot be stated yet that the lesions produced *in vitro* are the same as those produced *in vivo*. This conclusion will not be possible until general agreement has been reached on the significant characteristics of naturally caries lesions." In the General Biology of G. Alexander[82] we read: The kind of machine that would have to exist to provide an analogy with a living thing does not exist." A live tooth refuses to conform to a model *in vitro*.

CIVILIZATION AND CARIES

Dentists the world over are engaged in a bitter campaign against the ravages of caries, with the aim to save our natural teeth from impending decay and total loss.

In our measures of control we are guided by valid evidence that one of the major factors of the disease is retention of sticky precooked foods abundant in the daily ration of our civilized diet.

We speak of caries as "the price we pay for civilization." This is sad enough. But the needs of the evil are planted much deeper. It is in essence a campaign against evolution, the war we wage is in essence a war against the shape and arrangement of teeth as determined by a long process of evolutionary "adaptation." Thus, we are up against a disease which is continuously being aggravated by adversities of evolution as well as civilisation.

At the beginning of their career, early in their history, mammalian teeth were spaced, the shape of molars triconodont, the occulsion arranged in an alternate fashion. Such teeth offer no room for food retention; they are self-cleansing and open to "protective" salivary action. Carnivora retained their spaced teeth and arches with the triconodont molars, and they are caries-free. The gradual evolutionary changes of the human dentition have led to the reduction of the jaws and the evolvement of a closed arch, with proximal teeth in mutual contact, not always a perfect one. This favours food retention, sticky or fibrous: contacts loosen in time and change shape, gums recede with age, even in dentitions that previously have shown an "ideal" occlusion. Proximal cavities are among the worst and most damaging types of cavities, because

1. they are undermining
2. they ruin contacts
3. they affect the neighbour tooth
4. their restoration requires extension into the occlusal surface
5. their restoration requires more skill and is expensive; and
6. because of the danger of secondary caries.

It seems that the mutant gene or genes which brought about these changes in the course of evolution were in their main stream "lethal" to our dentition. This may be the cause why we are unsuccessful to hold in check the spread of caries, in spite of efforts, study and labor, thought and ingenuity.

But teeth became no longer vital for survival of homo sapiens. In the wake of civilization, natural foods were replaced by soft food, and prosthodontists perfected technics of man-made teeth: they have learned the art of concealing art. Teeth are constructed with due respect to esthetics, biology and whatever function is still required from them. In fairness, we ought not to blame caries on civilization, but to bless civilization for helping us to adapt the food to the present stage of evolution of our teeth.

May we conclude with the encouraging words of O. W. Holmes: "In opinions look not always back: Your wake is nothing, mind the coming track."

SUMMARY

Our knowledge of the factors and the mechanism of dental caries is imperfect, as is our understanding of the rare cases of immunity to caries, challenging as they may be. With all the achievements of nearly a century of caries research, enough questions remain to be answered. At times we have the impression that we did not progress very much since the days of Magitot, Miller, Black and other giants of the early period of dental research, in spite of a comprehensive literature and an abundance of data.

Until recently, caries initiation has been explained by two major theories mutually opposed. Enamel was for decades believed to be practically an inert structure, hence demineralization was considered tantamount to its total destruction. However, modern methods of investigation forced a completely different concept of enamel as basically dynamic. The emphasis on the organic structure became the hall-mark of the new research era, and our concepts of prophylaxis underwent a shift in emphasis: from the environment to the tooth structure. Accordingly, methods of prevention were advocated which aimed at the reduction (a) of enamel solubility (fluoridation), (b) its permeability (Gottlieb's prophylactic solution), or (c) at increasing individual resistance, systemic or local (diet, functional effort).

However, as long as we lack the knowledge of the essential steps in caries development, the current theories will be merely generalization formulas, and every attempt to attack the problem from a different aspect should be pursued with an open mind.

It was only natural, therefore, that all these vexing problems have precipitated a new theory of dental caries by another school of investigators, the so-called proteolysis-chelation theory, which explains the etiology of dental caries as two interrelated reactions integrated in one overall mechanism and occurring simultaneously. It presents in essence a wider amplification of repeated observations by many investigators that tooth decalicification may occur at a neutral or alkaline pH. A synthesis on a higher level of the phenomenon of chelation and proteolysis raises this new approach to a status of a comprehensive theory.

What we still need is a straightforward approach, unbiased by classical dogmas. One is reminded of Laban's suggestion: "We will call the damsel and inquire at her mouth."

In all, the broad nature of caries research presents an educational problem. Our prospective students should gain a more intimate knowledge of modern tools and methods of investigation as presently employed in biochemistry and biophysics.

Department of Anatomy,
School of Dentistry,
Hebrew University-
Hadassah Medical School,
Jerusalem, Israel

BIBLIOGRAPHY

1. Nuckolls, J., N. Y. State D. J. 18:17, 1952
2. Darling, A. I., Studies of the early lesion of enamel caries. Dr. D. J., 101:391, 1956.
3. De Vries, S. S., Taches blanches. Revue de Stomatologie, 57:24, 1956
4. Martin, J., Schatz A., and Karlson, K., Proteolysis-chelation: a new theory of dental caries. J. New Jersey State D.S., 27:7-8, 1955.
5. Rheinwald, Ulrich, Die Karies der Zaehne als Korrosionserscheinung. Johann Ambrosius Bart, Leipzig, 1956.
6. Sognnaes, R. F. and Wislocki, G. B., Histochemical obervations on enamel and dentin undergoing caries destruction. Oral Surg., O. Med., O. Path., 3:1283, 1950.
7. Miller, W. D., Microorganisms of the Human Mouth. S. S. White D. Mfg. Co., Phila. 1890.
8. Sullivan, H. R., Formation of early lesions in dental enamel. J.D.R., 33:229, 1954.
9. Symposium on Oral Bacteriology. J. Norw. D. A. Apr. 1956, p. 17-18.
10. McClure. F. J. and Ruzicka, S. J., Destructive effect of citrate vs lactate ions. J. D. Res., 25:1, 1946.
11. Nikiforuk, G. and Sreebny, L., Demineralization of hard tissues at neutral pH. J. D. Res., 32:866, 1953.
12. Bagnall, J. S. Trends in Caries Research. National Res. Council of Canada, p. 7, 1950.
13. Kantorowicz, A., Kariesrueckgang nach Einfuehrung der Rachitis Prophylaxe. Sch. Monatschr. Zahnheilk., 8:817, 1955.
14. Sullivan, H. R., Pathogenesis of dental caries. O.S.O.M.O. Path., 8:178, 1955.
15. Survey of the Literature of Dental Caries, publication 225, Nat. Ac. Sci., 1952, p. 82.
16. Roth, G., Proteolytic organisms of caries lesions. Oral Surg., O. Med., O. Path., 10: 1957.
17. Brudevold, F., J. D Res., 27:320, 1948.
18. Scott, D. B. and Albright, S. T., Electron microscopy of carius enamel. O. S., O. M., O. Path, 7:77, 1954.
19. Nuckolls et al., J.A.D.A., 44:529, 1952.
20. Klein, H., Physiochemical studies on the structure of dental enamel. J.D.R., 12:85, 1932.
21. Scharpenak, A. E., The role of piruvic acid and Vitamin B, in the development and prevention of dental caries. Stomatology (Russian) 37:3, 1958.
22. Hall, D. M., Enamel Structure by electron microscopy. J. D. Res., 37:252, 1958.
23. Sognnaes. R. F., Histochemical characteristics of the mineralized tissues. Annals of the New York Academy of Sciences 60:545-575, 1955.

24. Gottlieb B., Dental Caries. p. 71, 122, Lea and Febiger, Philadelphia, 1947.
25. Westin, Gosta, Histopathology of the enamel. Acta Odont. Scandinavica, 10:44, 1952.
26. Coolidge, T. B., an Jacobs, M. H., Enamel Carbonate in Caries J. D. Res., 36:765, 1957.
27. Land, M., Chalky enamel, Texas D. J., Oct. 1944.
28. Mandel, J. D., Histological, histochemical and other aspects of caries initiation. J.A.D.A., 51:437, 1955.
29. Schatz, A., Karlson, K. E., Martin, J. J., and Schatz, V.: Annals of Dentistry, 16:47, 1957.
30. Scott, D., Ussing, M., Sognnaes, R. F., Wyckoff, R. W., Electron microscopy of mature human enamel. J. D. Res., 31:74, 1952.
31. Losee, Fred L., Microlamellae in Enamel. Dental Radiography and Photography, 29:23, 1956.
32. Shaw, J., Nutrition and calcified tissues. J. D. Med., 9:19-22, 1954.
33. Fanning, R. J., Shaw, J. H. Sognnaes, R. F., Salivary contribution to enamel maturation. J.A.D.A., 49:671, 1954.
34. Sognnaes, R. F., Tooth Structure and Caries., Alpha Amega, Fall 1952, p. 2.
35. Losee, F. L. Jennings, W. H., Lawson, M. E. and Forziati, A. F., Microstructure of the human tooth. Naval Med. Res. Institute. 15:229-235. 1957. Research Report.
36. Scott, D., Optical microscopy of tooth surfaces. O.S., O.M., O. Path., 5:641, 1952.
37. Bernick, Sol., Baker, R. F., Rutherford, R. L., & Warren, O., Electron microscopy of enamel and dentin., J.A.D.A., 45:689, 1952.
38. Shaw, J. and Sognnaes, R. F., Advances in Experimental Caries Research. Am. Ass. for the Adv. of Sci., Wash., D. C., 1955, p. 98.
39. Bhussry, B. R. and Bibby, B. G., Surface changes in enamel. J. D. Res., 36:416, 1957.
40. Volker, J. F., and Klapper, C. E., Observations on dental caries in Syrian hamsters. Oral S., O.M., O.P. 7:211, 1954.
41. Beust, T. B., J.D.R., 12:601, 1932. Den. Cosmos, 76:305, 1934.
42. Neumann, H. H. and DiSalvo, N. A., Effect of disuse on the specific gravity of rat teeth, D.I.I., Sept. 1949.
43. DiSalvo, N. A., and Neumann, H. H., Physical characteristics of the diet and the water content of monkey teeth. J. Den. Res., 29:104, 1950.
44. Neumann, H. H., Lefkowitz, W., and Disalvo, N. A., Relation of function to Caries rate., J. D. Res., 26:182, 1947.
45. Frisbie, H. E., and Nuckolls, J., J. D. Res., 26:182, 1947.
46. Amprino, R., and Camanni, F., Autoradiographic Research on dental tissue. Acta Anatomica, 23:244, 1956.
47. Brahant, H. and Klees, L., Contribution a' l'etude de craqueures de l'email dentair humain. Actualites Odontontostomatologiques, 39:376, 1957.
48. Brudevold, F., Gardner, D. E., and Smith, F. A., Distribution of fluorides in human enamel. J. D. Res., 35:420, 1956.
49. Applebaum, E., Grenz-ray and tissue changes in dental caries. Annals of Dentistry, 7:70, 1948.
50. Verzár, F., The Ageing of Connective Tissue. Gerontologia 1:371, 1957.
51. Thewlis, J., Structure of teeth as shown by X-ray examination. Med. Res. Council, His Majesty's Stationer's Office, N238, London, 1940.
52. Barr, I. H. et al. Caries on different locations of teeth. J. D. Res., 36:544, 1957.
53. Applebaum, E., J.D.R., 11:616, 1931.
54. Atkinson, H. F., The permeability of human enamel. B.D.J., 84:119, 1948.
55. Bodecker, C. F., Enamel of the Teeth decalcified by the celloidin decalcifying method. Dental Review, 20:317, 1906.
56. Darling, A. I. (Discussion), Br. D. J., 93:286, 1952.
57. Manley, E. B., and Hardwick, S. L., Caries of the enamel. Br. D. J., 91:43, 1951.
58. Burnett, C. W., and Scherp, H. W., J. D. Res., 31:766, 1952.
59. Hurst, V., Nuckolls, S., Frisbie, H. E., Marshall, M. S., Initiation of enamel caries., O. Surg., O. Med., O. Path., 7:192, 1954. 6:976, 1953.
60. Guzman, C., Brudevold, F., and Mermagen, G., Soft roentgen-ray study of early caries lesion. J.A.D.A., 55:509, 1957.
61. Gottlieb, B., Diamond, M., and Applebaum, E.: The caries problem. A. J. Orth. and Oral Surg., 32:375, 1946.
62. Bartels, H. A., Trends in caries research. Oral Surg., O. Med., O. Path. 6:127, 1953.
63. Evans, D. G., Prophet, A. S., Disintegration of human dentin by bacterial enzymes. Lancet, 1:290, 1950.
64. Schatz, A., Karlson, K. E., Martin, J. J. and Schatz V., The proteolysis-chelation theory of dental caries. Odontologisk Revy, 8:154, 1957.
65. Gottlieb, B. A., New Concept on the Caries Problem. J.A.D.A., Nov.-Dec., 1944.
66. Pincus, P. 200, 1953 Brit. D. J. 84:25, 1948.
67. Wislocki, G. B. and Sognnaes, R. F., Histochemical reactions of normal teeth. Am. J. Anatomy, 83:239, 1950.
68. Atkinson, H. F. and Matthews, E., The organic components of the human tooth. Brit. D. J. 86:171, 1949.
69. Nuckolls et. al., Some recent studies concerned with fundamental research on beginning caries. J.A.D.A., 49:541, 1952.
70. Keil, A., Zeitschr. F., Zellforschung, 25:204, 1936.
71. Burnett, G. W., and Scherp, H. W., Accessibility of the protein dentinal matrix. J. D. Res., 31:788, 1952.
72. Gurkan, S. I., Application of Gottlieb,s prophylaxis in the treatment of deciduous teeth. Intern. D. J., 8:10, 1958.
73. Pincus, P. Production of dental caries, Brit. Med. J., 11:238, 1949.
74. Forscher, B. K. and Fosdick, L. S., Studies on physico-chemical phenomena related to dental caries. J. D. Res., 33:213, 1954.
75. Martin, J., Isenberg, H. Schatz, V., Trelawny, G., and Schatz A.: Euclides (Madrid) 14:313, 1954.
76. Muller, G., and Schait, A., Morphologic differences of repicas of intact Enamel decalcification in acid or E.D.T.A., HOA., Apr. 1957, p. 6.
77. Shaw, J., and Gupta, O., Chelation and smooth surface lesions. J. Nutrition, 60:320, 1956.
78. Pincus, P.: Further tests on human enamel protein, Biochem. J. 42:221, 1948.
79. McClure, F. J., Dietary factors in experimental rat caries. Advances in exper. caries research. Am. Association Advancement of Science, Washington, D. C., 1955, p. 122.
80. Pigman, W., In vitro production of experimental caries. J.A.D.A.. 51:685, 1955.
81. Gustafson, G., The histopathology of caries of human dental enamel. Acta Od. Scand., 15:13, 1957.
82. Alexander. G., General Biology, Crowell, N. Y., 1956, p. 21.
83. Thewlis, J., X-ray examination of human teeth. Br. D. J., 57:457, 1934.
84. Jarmer, K., Deutsche Stomatologie, 2:413, 1952.
85. Appleton, J. L. T., Symposium on the primary cause of dental caries. N. Y. State D. J., 18:3, 1952.
86. Orland et al., Germfree animal technic for study of dental caries. J. D. Res., 33:170, 1954.
87. Hals, Einar, Morch, T., and Sand, H. F., Effect of lactate buffers on dental enamel in vitro. Acta Od. Scand., 13: 94, 1955.
88. Ockerse and Jager, Brit. D. J., 102:96, 1957.
89. Zipkin, I., and McClure, F. J., Caries Potentiation and Sodium Dehydroacetate. Proc. S.E.B.M., 97:320, 1958.
90. Kronfeld, R., Histopathology of teeth and surrounding tissues. 4th Ed., revised by Paule Boyle. Lea and Febiger, Philadelphia 1955, p. 120.

LE NON-RESOLVITE PROBLEMA DEL CARIE DENTAL

per Dr. chir. dent. Jacob Yardeni

SUMMARIO IN INTERLINGUA

Nostre cognoscentia del factores e del mechanismo de carie dental es imperfecte, e le mesmo vale pro le rar casos de immunitate contra carie. Grande progressos ha essite effectuate in quasi un seculo de recercas in le problemas de carie, sed un abundantia de questiones remane a clarificar. A vices on ha le impression que le major progressos occurreva quasi omnes in le dies de Magitot, de Miller, de Black, e del altere gigantes del prime periodos del recercas dental, e isto in despecto de un vaste litteratura e un abundantia de nove factos.

Usque recentemente, il existeva duo major theorias pro explicar le initiation de carie, e iste duo theorias se excludeva mutualmente. Durante longe decennios, email esseva reguardate como un substantia practicamente inerte, e su dismineralisation esseva plus o minus identic con su destruction total. Tamen, moderne methodos de investigation ha imponite un satis differente conception in le qual le email es un substantia de character fundamentalmente organic. Le accentuation del structura organic deveniva le distinctive characteristica del nove recercas, e etiam nostre conceptiones del prophylaxe experientiava un displaciamento de lor centro de gravitate, i.e. ab le ambiente ad le structura del dentes mesme. Per consequente, nove methodos preventive esseva rcommendate, visante a reducer (a) le solubilitate del email (fluoration) e (b) le permeabilitate de illo (solution prophylactic de Gottlieb) e a augmentar (c) le resistentia individual —systemic e local (dieta, effortio functional).

Tamen, in tanto que nostre comprension del phases principal in le disveloppamento de carie remane imperfecte, le currente theorias debe remaner formulas de generalisation, e omne effortio de attaccar le problema ab un nove puncto de vista debe esser salutate con interesse active.

A generalmente parlar, le vaste natura del recercas de carie representa un problema educational. Nostre studentes debe ganiar un familiaritate plus intime con le moderne instrumentos e methodos de investigation como illos es usate currentemente in le campos del biochimia e del biophysica.

Book Reviews

Endodontics, by Harry J. Healey, A.B., D.D.S., M.S.D., F.A.C.D., C.V. Mosby Co., St. Louis, 370 pages, with 149 figures, 1960, $7.75.

There has been increasing emphasis on the art and science of endodontic therapy during the last two decades. High speed rotary techniques, full coverage in rehabilitation procedures, and the desire to retain teeth periodontally and endodontically involved, all have stimulated and stabilized endodontics so that it now plays a prominent part in the general practice of dentistry.

This book is an excellent guide for the student and practitioner to a more complete understanding of the details of endodontic techniques and a knowledge of how endodontics fits into the practice of dentistry.

The pocket size volume is one of the Postgraduate Dental Lecture Series. It should be in the library of every practitioner.

An Atlas of Dental and Oral Pathology, by Sydney Blackman, M.R.C.S., L.R.C.P., D.M.R.E. (Camb), John Wright & Sons, Ltd., Bristol, England. 372 pages, 816 illustrations, 1959, $15.00. (The Williams & Wilkins Co., Baltimore, exclusive U.S. Agents.)

This atlas is a photographic reproduction from films which have been taken during the last twenty-eight years in the X-ray Department of the Royal Dental Hospital, London, of patients seeking routine examination. This compilation is divided into three parts and numerous sections covering normal anatomical landmarks, tooth eruption, abnormal development, inflammatory conditions, traumatic involvements, and neoplastic formations. At the beginning of each section the conditions to be discussed are accompanied by an explanation of the underlying pathology, classification and sequence of spread and progress.

Each of the 816 illustrations is clear and is accompanied by a descriptive legend. This book is helping to meet the increasing needs and demands in dentistry and radiology to provide a reference book for fundamental interpretation of dental conditions.

Basic Periodontology, by A. Bryan Wade, B.Ch.D., F.D.S., R.C.S., John Wright & Sons, Bristol, England. 304 pages, 223 illustrations, 1960, $10.00. (The Williams & Wilkins Co., Baltimore, exclusive U.S. Agents.)

England's noted periodontist, Dr. A. Bryan Wade, has written a text for students and practitioners which is divided into three parts, Health, Disease and Prevention.

Dr. Wade believes that the student and practitioner must have an appreciation and understanding of the oral cavity in a state of health before proceeding to study in detail the oral tissues in disease. Without such a background the disease processes and the principles of treatment cannot be fully understood nor suitable preventive measures instituted.

In the section on Disease, etiology is discussed from the point of view of local and systemic factors. Pathology of the oral cavity is thoroughly reviewed. Diagnosis and treatment is covered in some 112 pages.

The last section of the text discusses Prevention which is the ultimate goal of dental therapy. The importance of maintenance through nutrition, function and cleanliness is stressed. These measures are necessary if we hope to be able to maintain the benefits derived through periodontal therapy.

Although this book cannot be compared in scope and content with the American counterparts dealing with periodontia, the subject is presented clearly and concisely by Dr. Wade in a systematic way. The reader will get an excellent understanding of periodontal etiology, diagnosis and treatment from this book.

Accepted Dental Remedies, 26th Edition, American Dental Association, Chicago, 244 pages, $3.00, 1961.

Accepted Dental Remedies 1961 is the twenty-sixth edition of a book that has become widely recognized as a handbook of dental therapeutics. The revised edition contains expanded sections on dental therapeutics. The monographs have been reviewed by the Council and its consultants and have been rewritten in the light of current scientific information. The chapter on "Fluoride Compounds" has been revised and expanded to include a discussion of the physiology of fluorides, fluoridated water, dietary fluoride supplements, topical application of fluorides, with particular reference to sodium fluoride solutions, and stannous fluoride. No changes have been made in the format which has proven so popular in the past several years.

Accepted Dental Remedies 1961 contains 244 pages, including the provisions for acceptance of products, a general index, a distributors' index, an index of current reports from the Council and the Division of Chemistry, and an index of more recent

reports on products not listed in the book, including those classified in Groups B, C and D.

The Science of Dental Materials, by Eugene W. Skinner, Ph.D., and Ralph W. Phillips, M.S., fifth edition, W. B. Saunders Co., Philadelphia, 636 pages, 1960.

In this fifth edition some radical changes have been made in almost every chapter. In this volume the discussions of the theoretical phases have not been greatly changed but the clinical applications have been considerably expanded.

Three new chapters have been added covering rubber base impression materials, tarnish and corrosion as related to dental problems, and a discussion of dental burs and high speed power sources. The subjects of cavity liners, calcium hydroxide cements, dentifrices and porcelain to gold restorations are included for the first time. The material on dental amalgam has been expanded to include a critical review of the clinical restoration and the factors which control its clinical success.

This is an excellent text for dental students and practitioners.

Theory and Practice of Crown and Bridge Prosthodontics, by Stanley D. Tylman, A.B., D.D.S., M.S., F.A.C.D. and Stanley G. Tylman, B.S., D.D.S., 4th edition, C. V. Mosby Company, St. Louis, 1474 illustrations and 11 color plates, 1960, $17.50.

Doctor Tylman's textbook has been considered "the bible" of crown and bridge for the last two decades. In this fourth edition the fundamental principles and methods that have been proved sound, both biologically and mechanically, have been retained. The chapter on the evolution and technic of high-speed tooth-cutting methods and equipment is entirely new. The chapter on the hydrocolloid impression materials has been revised in keeping with present-day knowledge of their manipulation and physical phenomena. The new chapter on the use of the mercaptan and silicone base impression materials is comprehensive in its discussion of the physical properties and manipulation of these materials. The revived interest in the use of porcelain baked directly to metal restorations merited an extensive description and discussion of this method when used for the construction of individual crowns and bridge restorations. The newer methods of firing porcelain under vacuum are fully discussed.

Another new chapter describes and illustrates in detail the step-by-step procedure of registering and recording the functional relations of the mandible with an adjustable face bow and with hinge axis registrations obtained with the new Hanau H2-XPR articulator.

This fine text should be in the library of everyone interested in crown and bridge prosthesis.

Practical Orthodontics, by George M. Anderson, D.D.S., Sc.D., and collaborator, Paul A. Deems, D.D.S., with three contributors, C. V. Mosby Co., St. Louis, 9th Edition, 719 illustrations, 1960, $18.00.

Practical Orthodontics starts with an introduction to orthodontics and ends with treatment aids and procedures which have proved of benefit through their application and use in the specialist's office. The manuscript was prepared to give a comprehensive view of orthodontic methods and aids not always available, because of time limitations to graduate students and to the preceptee who may be practicing in an office in which technical procedure are restricted to a single method. This comprehensive view indicates there is more than one way to do a thing. The pedodontist or the general practitioner of dentistry especially interested in the care of the child patient will find guidance in the prevention of malocclusion.

Since the last edition was published, there has been continued expansion in research and knowledge relating to the fields of etiology and diagnosis. Additional technical aids have become available for the planning of rational therapy. It is the new ideas and thoughts for which the author has gone far afield geographically that add to the value of this ninth edition. A skeletal classification of malocculsion, muscular functional disharmonies, the utilization of serial extraction, the use of removable plates, and the development of light wires forces indicate world wide activity among orthodontists to open new vistas and solve old problems.

The Dentist in Art, by J. J. Pindborg and L. Marvitz, Quadrangle Books, Chicago, 144 pages, illustrated, 1960, $12.50.

The Dentist in Art is a contribution both to esthetics and to our understanding of the development of dentistry in practice and as a profession. The excellent illustrations in this book display a great variety of artistic styles, medium and techniques in the hands of virtuouso craftsmen, from primitive vase paintings to the sophistication of modern sculpture, from drawings by Rembrandt and da Vinci to the satire of contemporary cartoonists. The pictures also demonstrate the growth of a body of true professionals using instruments functionally designed for dental purposes.

Previous contribution to "dental iconography" are very old and unobtainable. This volume is the first such work to be published in more than thirty years. It covers the full range of known materials, but the editors have drawn their selections largely from unfamiliar sources, avoiding the trite and irrelevant. Each of the illustrations is accompanied by an explanatory text, providing a witty, readable and authoritative account of the individual work of art, of its creator, and of its significance in the history of dentistry.

This unusual book is recommend to all interested in dentistry and art. It is excellent waiting room material for our patients.

Dentistry in the United States, Status, Needs and Recommendations, Summary Report of the Commission on the Survey of Dentistry in the United States, American Council on Education, Washington, D.C., 70 pages, 1960, $1.00.

Results of the most extensive survey of dentistry ever conducted in the United States were recently disclosed in this publication released by the American Council on Education.

The publication, entitled "Dentistry in the United States: Status, Needs, and Recommendations," contains the summary report of the Commission on the Survey of Dentistry in the United States.

Major recommendations of the Commission involving dental health, practice, education and research urge:

1. An all-out effort by scientific researchers to discover better means of protecting mankind against tooth decay, periodontal disease and other oral irregularities.

2. Augmented and continuing dental care for school children as well as methods of financing dental service for indigent and low-income groups.

3. Extension of fluoridation of community water supplies to the fullest practical extent.

4. An increase in the number of dentists, requiring dental schools at least to double the present rate of graduation by 1975.

5. A heightening of public appreciation of the importance of dental care not only for its own sake but because of its relationship to total health care.

Citing an "immense disparity between what we do and what we could do to bring proper mouth care to all," the Commission listed the following factors as most critical:

1. The American people set an "astonishingly low priority" on dental care.

2. The 90,000 practicing dentists simply are not enough to take care of the burgeoning population.

3. Despite the country's great wealth, many citizens are unable to pay for comprehensive dental care.

4. Dentists should make more extensive use of dental auxiliaries, such as assistants, hygienists and laboratory technicians.

To implement its recommendations, the Commission urged a 20-fold increase by 1972 in spending on capital expenditures for dental schools, support of these schools, fluoridation of community water supplies, care for school children and dental research.

In dollars and cents, this would mean the nation would spend about $1 billion a year on these matters compared with the present $45 million.

While recognizing the enormity of its financial recommendations, the Commission estimated that if all suggested programs were initiated in 1961, the peak per capita cost, coming in 1972, would be only about $4.80.

DENTAL EXTRACTION*

TO THE EDITOR:—*Is it generally conceded that all or most patients need prophylactic antibiotic treatment before dental extraction? What is the best antibiotic for prevention or treatment of postextraction infection?*

John J. Lorang, M.D., Tekoa, Wash.

ANSWER.—Prophylactic antibiotic therapy is neither necessary nor desirable before all dental extractions, but it is recommended prior to dental extractions, gingivectomy, or gingival curettage in patients who give a history of rheumatic heart disease or diabetes and patients receiving corticosteroid therapy. It may also be desirable if surgical procedures are required during the last trimester of pregnancy.

Penicillin is usually used, provided the patient does not give a history of penicillin sensitivity, in which event erythromycin or one of the tetracyclines can be given. If the penicillin is administered orally, 300,000 units of penicillin V every 4 to 6 hours for the 24 hours preceding the operation and for 96 hours thereafter can be given. This subject is discussed in greater detail in *Accepted Dental Remedies, 1960.*

LESTER W. BURKET, M.D., D.D.S.

* Questions and Answers, J.A.M.A., Nov. 26, 1960, p. 1760.

Academy Proceedings

MASSACHUSETTS SECTION

A full day Fall meeting of the Massachusetts Section was held Sunday, October 24th at the Veteran's Administration Hospital in Boston under the new corps of officers; Dr. Richard C. Harriott, President; Dr. Maurice F. Grossman, President-elect; Dr. Robert I. Diamond, Vice President; Dr. Edward R. Loftus, Secretary, and Dr. Charles V. Calderone, Treasurer.

Dr. Leslie Milne, chairman of arrangements, presented the program designed to acquaint the practitioner with hospital procedures and techniques. In the morning, Stephen P. Mallett, D.M.D., F.A.C.D., former chief of dental service at Boston City Hospital, and lecturer at Tufts University School of Dental Medicine, presented his paper, "Preparation of the Patient and Operating Room Procedure." Following the presentation of the paper, Dr. Mallett, using the teaching operating room, went through the complete operating room procedure, assisted by the staff of the hospital, and with commentary by Dr. Milne.

Following a roast beef dinner prepared and served by the Hospital, our National Secretary, Dr. George F. Clarke spoke of the work of the Academy at the national level. Dr. Earl Stone, as the Chairman of the Graduate Award Committee, spoke of the contacts the Academy is making with the dental schools of the nation. Our delegate, Dr. Leslie Milne spoke of the last National meeting in Philadelphia. It was unanimously voted to invite our President, Dr. Hermann Becks, to make his fraternal visitation to our section.

In the afternoon, Donald Mahler, M.D., Chief of Anesthesiology of the Veteran's Administration Hospital of Boston, and Professor at Tufts University School of Medicine presented a paper "Anesthesias, Pre-Medication, and the 'Caine' Sensitivity Reactions." A question and answer period followed this talk.

MONTREAL SECTION

The Annual Meeting of the Montreal Section of the Academy was held on April 27, 1960 at the Cercle Universitaire. After a delightful dinner with our womenfolk, the elections of officers took place with the following results:

President	Dr. P. J. Gitnick
Vice President	Dr. H. M. Robichaud
Secretary	Dr. R. F. Harvey
Members of the Executive	Dr. R. M. Wiener
	Dr. G. Plamondon
	Dr. A. D. Richardson
	Dr. H. T. Oliver
Section Delegate	Dr. L. J. Rosen

The evening terminated with the showing of a first run film.

On September 12, 1960 the first scientific meeting was held at the Mount Stephen Club. The guest lecturer was Dr. Claude Bertrand, Chief Neurosurgeon, Notre Dame Hospital, Montreal and President, Canadian Neurological Society who spoke on "The Intriguing Principles of Facial Pain."

The next meeting will he held on November 28th at the Cercle Universitaire. The guest lecturer will be our own member Dr. R. M. Wiener who will discuss "Minor Oral Lesions."

LOUIS J. ROSEN, *Delegate*

MISSOURI SECTION

The Missouri Section had a successful meeting on September 12, 1960. The speaker was Dr. Louis Tureen, the head of the neurology department at St. Louis University Medical School. His topic: "The Neurologist and Dentist."

On November 28th a meeting was held with Dr. George G. Stewart as the speaker. The title of his lecture was "Focal Infection." The meeting was open to all medical and dental men in this community and was to be held in conjunction with the Mid-continent Dental Congress. The Section sponsors this meeting at the Jewish Hospital Steinberg Auditorium.

GUNTER SCHMIDT, *Delegate*

AMERICAN ACADEMY OF DENTAL MEDICINE NEW MEMBERS ELECTED AT BUSINESS MEETING, DECEMBER 4, 1960

Bauxbaum, Jerome
Glen Burnie, Md.

Belsky, Maurice
New Brunswick, N. J.

Calle-Restrepo, Carlos
Medellin, Colombia, S. A.

Cording, Robert C.
Dearborn, Michigan

Frank, Harry J.
Philadelphia, Pa.

Gilbert, Harold
Baltimore, Md.

Goldberg, Howard
Baltimore, Md

Goodfriend, David J.
Philadelphia, Pa.

Greer, T. B.
Houston, Texas

Gudwin, Morris H.
Flushing, N. Y.

Gunter, John L.
Columbia, S. C.

Highstein, Norman
Baltimore, Md.

Hinds, Eugene
Baltimore, Md.

Leone, Edward F.
West Allis, Wisc.

Light, Jerome E.
Armonk, N. Y.

McCrossen, Edward
Brooklyn, N. Y.

Merrick, Stephen
Brooklyn, N. Y.

Mittelman, Jerome S.
New York, N. Y.

Phillips, Frank J. F.
Brockville, Canada

Pollack, Alfred
Brooklyn, N. Y.

Riggs, Herbert P.
Daytona Beach, Fla.

Sager, Robert Henry
Chapel Hill, N. C.

Salisbury, Frederick
Richmond, Va.

Sheridan, Roland C., Jr.
San Francisco, California

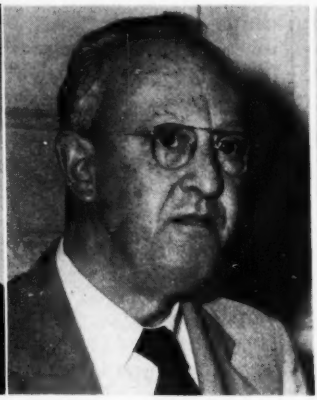
Simon, Robert S.
Clayton, Missouri

Steward, John P. (Associate)
Palo Alto, California

Sweren, Edgar
Pikesville, Md.

ACADEMY MEMBERS RECEIVE FULBRIGHT GRANTS

Dr. Martin Entine



Dr. S. Leonard Rosenthal

Dr. George G. Stewart

The Department of State has notified three of our members that they have been awarded grants to teach in 1961. The scene of their activities will be the School of Dentistry, San Marcos University at Lima, Peru.

The grantees, all members of the Philadelphia Section are:

Dr. Martin Entine, Lecturer in Oral Pathology at Temple University, who will present a course in Occlusal Rehabilitation and Crown and Bridge Prosthesis April 15-June 14;

Dr. S. Leonard Rosenthal, Professor of Oral Diagnosis at Temple University, who will teach Oral Medicine and Diagnosis June 15-August 14;

Dr. George G. Stewart, Assistant Professor of Oral Medicine at the University of Pennsylvania, who will give a course in Endodontics August 15-October 14.

All courses will consist of lectures, demonstratoins and clinical instruction and will be conducted entirely in Spanish.

La Universidad Nacional Mayor de San Marcos de Lima is the oldest university in the western hemisphere. Founded by the Spanish in the early 16th century, it is the center of Peruvian culture and one of the largest institutions of learning in South America. The Dental School has been completely reorganized by the new Dean, Frederico Schuetz.

There have been few Fulbright Commission teaching grants to dentists in the past. They were limited to those who could serve for 6-12 months. The Committee on International Interchange in Dental Medicine convinced the Commission that this was impossible for most dentists and that short term grants for a teaching team would be more practical. The present grants which provide for travel, living expenses and costs of dependents are the first under the new policy. Other Latin American countries have shown lively interest in the program; so that the Academy can serve widely if a sufficient number of Spanish-speaking members are available.

The Philadelphia Society of Periodontology

in conjunction with

The Philadelphia Chapter of the American Academy of Dental Medicine

Presents

THE SEVENTH ANNUAL ALL-DAY MEDICAL MEETING
WEDNESDAY, FEBRUARY 15, 1961

SUBJECT: Diabetes—Its Relationship to Dentistry

AFTERNOON MEETING: University of Pa. Dental School—40th & Spruce Sts.—1:30 P.M.

PANELISTS: *Joseph T. Beardwood, Jr., M.D.*
Professor of Metabolic Diseases, Graduate School of Medicine, Univ. of Pa.
TITLE: Pathologic Physiology of Diabetes
TIME: 1:30 to 2:30 P.M.

Norman G. Schneeberg, M.D.
Associate Professor of Medicine, Temple Univ. Medical Center; Chief of Endocrinology of the Phila. General Hosp. and Einstein Medical Center.
TITLE: Clinical Aspects of Diabetes
TIME: 2:30 to 3:30 P.M.

Emanuel Cheraskin, D.M.D., M.D.
Professor of Oral Medicine, Univ. of Alabama Medical Center
TITLE: Diabetes—Its Relationship to Dentistry
TIME: 3:30 P.M.

EVENING MEETING: Begins promptly at 7:30 P.M.

PANELISTS: Emanuel Cheraskin, D.M.D., M.D.

TITLE: Research Findings in Diabetes.

The most recent clinical and research findings in Diabetes will be presented by an outstanding panel of teachers and clinicians.

Physician and Dentist cooperation is essential in treatment of the Diabetic patient. This all-day session should be most rewarding to members of both professions.

Fee, Including Dinner
Members $20.00
Non-members $25.00
Students $5.00 (does not include dinner)

For Reservations: Contact
Dr. Emanuel Malamed, Sec'y
1147 Magee Avenue,
Philadelphia 11, Pa.

THE NEW YORK SECTION

The New York Section is anticipating one of its most active and exciting years in the history of the Academy. In addition to a stimulating program of local meetings it will be host at both the December meeting and the 1961 National Cruise Convention.

The following are the officers and committee chairman for 1960-1961:

President ..... Dr. Henry I. Greene
Pres. Elect ..... Dr. Angelo Cacciatore
Secretary ..... Dr. Seymour Koteen
Treasurer ..... Dr. Leonard Nevins
Asst. Editor ..... Dr. Alan Simonson
Editor ..... Dr. Arthur S. Nachbar
Delegate ..... Dr. Howard L. Ward
Trustees ..... Dr. Celia Dickman, Dr. David Disick, Dr. Frederick Romberg

Committee Chairmen

Membership ..... Dr. Arthur Nachbar and Dr. Stanley Miller
Constitution ..... Dr. Frederick Romberg
Program ..... Dr. Frederick Romberg
Past Presidents ..... Dr. Howard L. Ward

On the local level, the Program Committee has planned to have new material presented by enthusiastic lecturers to help stimulate attendance at meetings. The basic theme for this year's programs will be "Occlusion," with presentations on the various schools of thought. The speaker at our first meeting on November third was Dr. Frank V. Celenza, who discussed "Current Developments of Gnathological Philosophy."

On the national level, the December Meeting was planned under the able Chairmanship of Dr. Stephen Nachbar. Dr. Howard L. Ward is the General Chairman of the 1961 National Cruise Convention.

DR. HOWARD L. WARD, *Delegate*

DISTINGUISHED ACADEMY MEMBER CITED PROFESSOR J. S. LANDA, THREE OTHERS HONORED

Dr. Joseph S. Landa was one of four dentists honored by Trinity College of Dublin at their June 1960 Graduation ceremonies. The four dentists were the first of their profession to receive honorary degrees from this institution.

The degree of Sc.D. was awarded to Dr. J. S. Landa (N.Y.C.), Dr. Holly Broadbent (U.S.A.), Dr. A. Lundstrom (Sweden), and Dr. Wilfred Fish (Great Britain).

After having received his D.D.S. (Magna Cum Laude) from the Imperial University of Odessa, Russia, in 1914, Dr. Landa graduated from N.Y.U. College of Dentistry in 1925, and taught at that school for 33 years (1925-1958). In 1959 he retired as Professor in charge of Prosthodontics and Cleft Palate Rehabilitations.

Dr. Landa is the author of two textbooks and numerous articles, as well as chapters in various additional texts. He won the Lord Chaim Prize in 1953 for an original research paper. In 1955 he was Fulbright Professor and lecturer at the Tokyo Medical and Dental University in Japan.

To quote the Provost of Trinity College as he conferred the degree upon Dr. Landa, "Both the Eastern and Western hemispheres of the globe can take credit for the benefits conferred on dental science by the work of honorary graduate Joseph Simeon Landa."

MICHIGAN SECTION

The Michigan Section of the American Academy of Dental Medicine held a dinner meeting September 27, 1960 in Detroit. Our meeting was held at the New Whitney House, which is the headquarters for the Wayne County Medical Society.

Following cocktails and dinner we heard Dr. Raymond Monto, Chief of the Hematology Section of Henry Ford Hospital in Detroit. Dr. Monto brought to our attention again the importance of the oral cavity as a barometer of general health, and as an aid in diagnosing correctly systemic disease and disorders. Of particular interest were his slides on cells from the oral cavity that could be diagnosed as cancerous, but were in reality changes due to anemias. In short, a good dinner, fine speaker, in very beautiful surroundings.

JOHN E. HANNAN, JR.

NEW JERSEY SECTION

The New Jersey Section of the Academy held a dinner meeting October 4, 1960, at the Hotel Douglas, Newark, New Jersey. Our Clinician was Daniel Brower, PH.D. a Clinical Psychologist. This meeting was the one meeting of the year at which the wives are invited. Dr. Brower offered to the group the following:

1. The Patient's anxieties should be warmly accepted and emphatically shared rather than rebuffed or verbally denied, let alone having the patient feel guilty, foolish or embarrassed for his anxiety; in such instances the guilt must turn into hostility toward the dentist, further fear of him and more hostility in a vicious circle.

2. One should not switch one's role with a given patient too rapidly, e.g. a helpful father, a demanding father, a brotherly co-equal, a warm but mild friend, etc. Each patient thrives best on a particular role and its maintenance.

3. In dealing with children, gauge the mode of handling through an appraisal of the mother and the mother-child relationship. With a child—take your time, do not fool him, talk to him at eye level, let him feel size of instruments and their texture, show him pictures of teeth.

We are awaiting word of the visitation by Dr. Becks to our section for our February meeting. At this meeting we intend to present placques to our Past Presidents. The membership approved the application of Dr. Maurice W. Belsky, 92 Carroll Place, New Brunswick, N. J.

The membership is being reached by means of bulletins, letters and telephone calls to stimulate attendance at the Section, Mid-Winter and Annual Meetings. From the enthusiasm demonstrated at our first meeting of the year we look forward to an active well attended series of meetings.

REUBEN FELTMAN, *Delegate*

REPORT OF THE MEMBERSHIP COMMITTEE

The Membership Committee has passed on 27 nominees and present them for your approval. It is interesting to note that 25% of the nominees were Academy Award Winners in their senior class. The geographic distribution of the members of this committee has been very advantageous especially where a more thorough investigation of nominee is necessary. It is the duty of, not just the Membership Committee, but all members of the Academy to watch for and invite those members of our profession who are outstanding and would be good Academy members.

Through the combined efforts of the Planning Committee and the Membership Committee the Information Booklet is printed. Even in this short time it has been a great help to this committee when prospective nominees ask for more information about the Academy. Booklets have been mailed to all officers, all members of the Membership and Planning Committees, and to all others who requested them. I wish to thank all members of both committees, for their ideas, advice and criticism, and especially Dr. Don Lyons. Without his help it would have been very difficult. Copies are available for those who desire them.

CHARLES M. CONAT, *Chairman*

REPORT OF THE INTERNATIONAL INTERCHANGE OF DENTAL MEDICINE COMMITTEE

Your committee is happy to report that the State Department and the Fulbright Commission in Peru have given final approval of three grants to members of the Academy.

Dr. Martin Entine, Dr. George Stewart and Dr. Leonard Rosenthal will give courses at San Marcos University in Lima Peru in 1961. Dr. Entine will teach occlusal reconstruction April 15-June 14; Dr. Rosenthal will present oral medicine June 15-August 14; Dr. Stewart will given endodontics August 15-October 14. The project brochure of the U.S. Department of State gives generous acknowledgement to the Academy of Dental Medicine for the program.

In addition, your chairman has accepted a suggestion to go to Bogota, Colombia, to attempt to arrange a program at the National University for 1962.

During the year, Academy members have spoken in many countries. Dr. Samuel Turkenkopf lectured around the world. Drs. Jacoby Rothner and Leonard Rosenthal in Tokyo, Japan and Bangkok, Thailand; Dr. George Stewart in Nicaragua. Dr. Don Lyons is now in the Far East.

Now that the path has been opened, it will be easier to obtain Fulbright funds. The Commission is especially interested in Latin America. It is necessary to have many more volunteers if we are to continue this project.

S. LEONARD ROSENTHAL, *Chairman*

Announcements

POSTGRADUATE TRAINING IN PERIODONTIA AND ORAL MEDICINE NEW YORK UNIVERSITY COLLEGE OF DENTISTRY

The following postgraduate courses in Periodontia and Oral Medicine will be offered at the New York University College of Dentistry and will be given by Dr. Sidney Sorrin and associates:

No. 124.02. REFRESHER COURSE IN PERIODONTIA AND ORAL MEDICINE

Ten sessions, Wednesday, 4:00 to 6:00 P.M. March 1, 1961 to May 10, 1961.
Tuition and books. $156.00. Instruments approximately $55.00.

Theoretical and practical application of periodontal diagnosis and techniques to general dentistry. Four lecture and six clinical demonstration sessions. Equilibration of occlusion is performed by the student on casts. Patient demonstrations include equilibration of occlusion, conservative and radical therapy, home care, etc.

No. 123.02. PERIODONTIA AND ORAL MEDICINE IN THE SPANISH LANGUAGE

Four weeks, Monday through Friday, 9:00 A.M. to 4:00 P.M.
April 10 to May 5, 1961 inclusive. Tuition including books and instruments approximately $385.00.

Theoretical and practical application of Periodontia and Oral Medicine is fully explained and demonstrated. Equilibration of occlusion is performed by the student on casts. Lectures and clinical demonstrations of diagnosis and treatment planning, conservative and radical techniques, equilibration of occlusion, home care, etc. The entire course is conducted in the Spanish language.

COMPREHENSIVE PREPARATION IN PERIODONTIA AND ORAL MEDICINE

No. 120.11 and 121.11. Two academic years, full time, September 19, 1960 to May 25, 1962.
Tuition $2,020.00 (two years). Instruments and books approximately $231.00.

No. 120.21 & 121.21 Four academic years, half time. September 19, 1960, to May 1964. (Two and one half days weekly.)
Tuition $2,020.00 (four years). Instruments and books approximately $231.00.

These courses are designed for comprehensive preparation in Periodontia and Oral Medicine and are of particular significance for certification towards specialization. All didactic and clinical phases are covered with the objective of developing expert proficiency.

No. 222. GRADUATE COURSE IN PERIODONTIA AND ORAL MEDICINE

Two academic years, full or half time, beginning Sept. 19, 1960. Tuition $2,020.00. (two years). Instruments and books approximately $275.00.

This program leads to the degree of Master of Science (in Dentistry). The objectives are to teach superior proficiency in Periodontia and Oral Medicine based on adequate background in the basic sciences.

For further information, write to the Secretary, Postgraduate Studies, New York University College of Dentistry, 421 First Ave., New York, N. Y.

NEW YORK UNIVERSITY COLLEGE OF DENTISTRY

Refresher Lecture Series:

New York University College of Dentistry Alumni Association Refresher Lecture for February to be given at the Dental College 421 First Avenue, at 25th Street, Tuesday, February 14th, 1961, 8 P.M.

Dr. Andrew Cannistraci—"Simplified Accurate Impression Techniques for Fixed Partial Prosthesis"

Dr. Abram I. Chasens—"The Integration of Periodontics and Restorative Dentistry"

Chairman: Dr. Barry Tackler.

Parents Association:

Annual Affair of the Parents Association of New York University College of Dentistry.

At the Tavern on the Green, Central Park West at 67th Street, N.Y.C. Monday evenings, March 6th 1961, 6:30 P.M. $5.00 per person.

Dr. and Mrs. Carroll V. Newsom will be the honored guests.

ALBERT EINSTEIN COLLEGE OF MEDICINE YESHIVA UNIVERSITY DEPARTMENT OF DENTISTRY

The Department of Dentistry of the Albert Einstein College of Medicine of Yeshiva University announces the following postgraduate courses:

Anesthesiology DPD 11—Pre-medication, Co-medication and Supportive Therapy in Dental Practice. Dr. Stanley R. Spiro and Associates. April 6 and 7, 1961. $60.00.

Anesthesiology DPD 19—Preoperative and Pre-Anesthetic Evaluation Techniques for all Dental Patients. Dr. Stanley R. Spiro and Associates. June 9, 1961. $30.00.

Endodontics DPD 22—Dr. Julius Fox and Associates. February 22, 23, 24th, 1961. $100.00.

Dento-Alveolar Surgery DPD 33—Drs. Herbert Calman, Stanley J. Behrman, William Rakower and Associates. May 4, 5th, 1961. $50.00.

Oral Pathology and General Practice DPD 27—Dr. Ernest Baden, March 24, 31, 1961. $50.00.

Advanced Oral Pathology DPD 29—Dr. Ernest Baden and Associates. 3 consecutive days, December, 1961. $75.00.

Periodontics DPD 66—Drs. Marvin N. Okun, Irving Yudkoff and Associates. 10 Wednesdays, March 1st through May 3, 1961. $225.00.

Periodontics DPD 69—Drs. Irving Yudkoff, Marvin N. Okun and Associates. Oct. 30, 31st, Nov. 1, 2, 3rd, 1961. $175.00.

Prosthodontics DPD 77—Drs. Lester E. Rosenthal and Max A. Pleasure. (Full Denture Construction) Friday mornings, March 3, 10, 17, 24 and 31st, 1961. $75.00.

For further information and application blanks about specific postgraduate courses write to Director, Postgraduate Dental Division, Albert Einstein College of Medicine, Yeshiva University, Eastchester Road and Morris Park Avenue, Bronx 61, New York.

TEMPLE UNIVERSITY SCHOOL OF DENTISTRY GRADUATE AND POSTGRADUATE PROGRAM FOR 1960-61

Implant Dentures
Aaron Gershkoff, B.S., D.D.S. & Norman I. Goldberg, D.D.S.
January 9-13, 1961
Tuition: $200.00.

Anatomy—Head and Neck Dissection
Richard M. Snodgrasse, Ph.B., M.A., Ph.D.
February 1 to May 17, 1961 (Fifteen Wednesdays from 1 to 5 P.M.)
Tuition: $300.00. Enrollment limit: 6

Advanced Fixed Prosthesis
George Straussberg, D.D.S.
February 6-11, 1961
Tuition: $200.00. Enrollment limited

Present Day Periodontal Practice
Jacoby T. Rothner, D.D.S., Irving Glickman, D.M.D., Bernard Saturen, D.D.S., and Neal W. Chilton, B.S., D.D.S., M.P.H.
Tuesday, February 14 through Tuesday, April 18, 1961 (1 day a week for 10 weeks)
Tuition: $250.00. Enrollment limit: 10

Practice Administration
Jay H. Eshleman, D.D.S., D.Sc.
February 18, 1961
Tuition: $25.00. Enrollment limit: 20

Periodontal Prosthesis
Morton Amsterdam, D.D.S., F.A.C.D., & D. Walter Cohen, D.D.S. and Associates
Tuition: $275.00. Enrollment limited

Electronic Electrosurgery
Maurice J. Oringer, D.D.S.
March 3, 4, 1961
Tuition: $60.00. Enrollment limited

Immediate Surgical Endodontics
Leonard Parris, D.D.S., Harold Rappaport, D.D.S. and Robert Uchin, D.D.S.
March 6-10, 1961
Tuition: $175.00. Enrollment limit: 8

Advanced Surgical Techniques in Periodontal Therapy
Saul Schluger, D.D.S. and Jack Alloy, D.D.S.
March 20-25, 1961
Tuition: $300.00. Enrollment limit: 10

Full Denture Prosthesis
Bernard Jankelson, D.M.D. and Associates
May 8-12, 1961
Tuition: $200.00. Enrollment limited

Graduate Orthodontics
Robert B. Hedges, D.D.S., M.S., F.A.C.D., and Associates
September 7, 1961—A two year course
Tuition: $450.00 per semester.

For an application and further information, write to: Dr. Louis Herman, Director of Postgraduate Studies, Temple University School of Dentistry, 3223 North Broad Street, Philadelphia 40, Pennsylvania.

FIRST DISTRICT DENTAL SOCIETY

Bite Planes, Provisional Ligatures and Splints, Dr. Abraham Berliner, January 4, 5, 6, 1961, 10:00 A.M. to 4:30 P.M.

The Biodenture Technique, Dr. A. Milton Bell, January 5, 6, 7, 1961, 9:30 A.M. to 4:30 P.M.

Practical Endodontics, Dr. Samuel Luks, January 11, 18, 25, February 1, 1961, 1:30 P.M. to 4:30 P.M.

Improving Your Practice Through Effective Speech, Mrs. Grace Kirsten, January 13, 20, 27, February 3, 1961.

Practical Operative Dentistry, Dr. Charles Fower, January 13, 14, 1961, 10:00 A.M. to 4:30 P.M.

Dentistry for the Handicapped and the Behavioral Problem Patient, Dr. Jerry J. Adelson, January 18, 19, 20, 1961, 10:00 A.M. to 4:30 P.M.

Factors Governing Successful Oral Reconstruction, Dr. Harold Gelb, January 19, 20, 1961, 10:00 A.M. to 4:30 P.M.

Practical Radiodontics, Dr. Joseph J. Martini, January 25, 1961, 9:30 A.M. to 4:30 P.M.

Removable Precision Bridge Techniques in Reconstruction, Diagnosis and the Approach Treatment, Dr. I. Franklin Miller, January 24, 25, 26, 27, 28, 1961, 10:00 A.M. to 4:30 P.M.

For further information and applications, please write to the Postgraduate Department, First District Dental Society, Hotel Statler Hilton, New York City 1.

AMERICAN INSTITUTE OF ORAL BIOLOGY CASE HISTORY SERVICE

The Institute continues to offer Case Histories from the broad field of Oral Biology for the year 1960-61. These will include original 35 mm. Kodachrome slides of pathologic conditions of the oral cavity and jaws, accompanied by pertinent laboratory findings, medical background, roentgenograms, photomicrographs, diagnostic criteria and whatever else may be indicated in each individual case, with a general discussion" of the disease. A loose leaf binder and matching Kodachrome slide box will be furnished. The fiscal year of the Institute runs from October 1 to September 30.

This monthly service was initiated in 1952 and has met with outstanding success. During these eight years it has provided a total of 1200 one-year subscriptions and the histories were accompanied by 208 slides.

The subscriber to this Case History Service is entitled to full membership in The American Institute of Oral Biology. Members of the A.D.A. or A.M.A., or their foreign equivalent, are eligible to apply. Due to the great demand for this Service, it is recommended to subscribe at an early date for immediate delivery. An index of the various diseases covered during this period will be mailed upon request. Complete series for the 1954-59 are still available; unfortunately the series for 1952 and 1953 are out of print.

For further information, address all communications to the secretary, Mrs. C. Novembri, 2240 Channing Way, Berkeley 4, California.

UNIVERSITY OF ALABAMA SCHOOL OF DENTISTRY

The following courses will be offered at the University of Alabama School of Dentistry during the months of February, March and April:

February 11 and 12: "Dental Assisting": Paul E. Hammons, M.S., D.D.S.; Gertrude M. Sinnett, B.S., D.H.

February 18, 19, and 20: "Removable Orthodontic Appliance Construction" (Limited to practicing orthodontists): Samuel D. Gore, D.D.S.

February 24, 25, and 26: "Clinical Oral Surgery and Applied Oral Pathology": Charles A. McCallum, D.M.D., M.D.; Leonard Robinson, D.M.D., M.D.

March 10, 11, and 12: "Complete Denture Prosthesis": William L. McCracken, D.D.S., M.S.

April 8, 9, and 10: "Hypnosis Applied to Dentistry": William T. Heron, A.B., M.A., Ph.D.

April 15 and 16: "Management of Advanced Periodontal Disease": John F. Prichard, D.D.S.

For further information, please write to: Dr. Arthur H. Wuehrmann, Acting Dean, University of Alabama School of Dentistry, Birmingham 3, Alabama.

NEW YORK UNIVERSITY COLLEGE OF DENTISTRY REFRESHER LECTURE SERIES

New York University College of Dentistry Alumni Association Refresher Lecture for January will be given at the Dental College, 421 First Avenue at 25th Street, New York City, on Tuesday, January 17th, 1961 at 8 P.M.

Dr. J. A. Salzmann: "Orthodontic Principles in General Dental Practice." Chairman: Dr. Maurice Saklad.

FEDERATION DENTAIRE INTERNATIONALE ALBERT JOACHIM INTERNATIONAL PRIZE

Manuscripts from candidates for the Albert Joachim International Prize must be received by the Secretary General of the Fédération Dentaire Internationale, 35 Devonshire Place, London, W.1, England, not later than 1st July 1961. These will be considered by the international jury appointed by the Federation and the award will be made at the XIIIth International Dental Congress to be held in Cologne, Germany, 7th-14th July 1962.

Attention is drawn to the fact that the rules for this Prize have now been amended and as a result both published and unpublished theses on original scientific research of a laboratory or clinical nature in the field of odonto-stomatology carried out not longer than five years previous to July 1961, are eligible for the Prize.

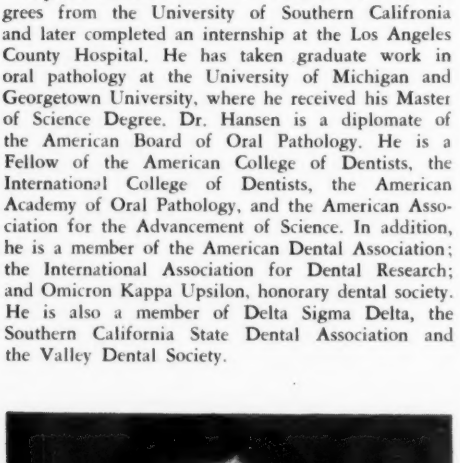
The 1962 award will consist of 50,000 Belgian francs (just over £300).

The full set of rules is obtainable on request from the Secretary General of the FDI, 35 Devonshire Place, London, England.

CHIEF, DENTAL AND ORAL PATHOLOGY DIVISION APPOINTED

Captain Louis S. Hansen (DC) U.S.N. has been appointed Chief of the Dental and Oral Pathology Division at the Armed Forces Institute of Pathology, Washington, D. C. He is the first naval officer to head an Institute Division. Dr. Hansen relieves Major General Joseph L. Bernier (DC) U.S.A. who was recently detached to assume the duties of Chief of the Army Dental Corps.

Captain Hansen received his B.S. and D.D.S. degrees from the University of Southern Califronia and later completed an internship at the Los Angeles County Hospital. He has taken graduate work in oral pathology at the University of Michigan and Georgetown University, where he received his Master of Science Degree. Dr. Hansen is a diplomate of the American Board of Oral Pathology. He is a Fellow of the American College of Dentists, the International College of Dentists, the American Academy of Oral Pathology, and the American Association for the Advancement of Science. In addition, he is a member of the American Dental Association; the International Association for Dental Research; and Omicron Kappa Upsilon, honorary dental society. He is also a member of Delta Sigma Delta, the Southern California State Dental Association and the Valley Dental Society.



Captain Louis S. Hansen (DC) U.S.N.

Captain Hansen is a veteran of 19 years naval service. His last duty station was the U. S. Naval Dental School, National Naval Medical Center, Bethesda, Maryland, where he was engaged as a dental researcher and an instructor in oral pathology.

TUFTS UNIVERSITY SCHOOL OF DENTAL MEDICINE

Tufts University announces three full-time graduate courses in Periodontology under the direction of Doctor Irving Glickman.

I. *PERIODONTOLOGY I:* This is a two-year (two academic years of eighteen consecutive months) specialist training program for individuals interested in qualifying for certification in Periodontia. It has been arranged in conformity with the requirements of the American Board of Periodontology.

II. *PERIODONTOLOGY II:* This is a one-year specialist training program, is a modification of the two-year course and is offered for individuals with a year's previous graduate or postgraduate training in Periodontology.

III. *PERIODONTOLOGY III:* This program is intended for individuals with a primary interest in the academic and research aspects of Periodontology. It is an eighteen-months course leading to the degree of Master of Science or Master of Dental Science.

DPG 606—"A Special Participation Course in Periodontology"

Monday through Friday for one week from April 24, 1961 through April 28, 1961
Tuition $175—Class Limited
Dr. Irving Glickman and Staff.

For information please write: Director, Division of Graduate and Postgraduate Studies, School of Dental Medicine, Tufts University, 136 Harrison Avenue, Boston 11, Massachusetts.

UNIVERSITY OF PENNSYLVANIA SCHOOL OF DENTISTRY RESEARCH AND TEACHING TRAINEESHIPS

Research and Teaching Traineeships in the basic sciences, in periodontology and in the comprehensive treatment and rehabilitation of the cleft palate patient are available at the School of Dentistry, University of Pennsylvania.

Candidates for the traineeships in the basic sciences must qualify for admission to the Graduate School of Arts and Sciences. These traineeships may lead to M.S. or Ph.D. degrees.

The traineeship in periodontology is a 2 year program devoted to basic science studies, clinical practice and research. It is intended primarily for those individuals who wish to enter into teaching and research in periodontology.

The traineeship in the comprehensive treatment and rehabilitation of the cleft palate patient is clinically oriented; however, opportunities for coursework in fields related to cleft palate therapy are available.

All traineeships are supported by the U.S. Public Health Service. Annual stipends vary from $4,500 and up depending on the qualifications and needs of the successful candidates. Inquiries for the basic science and cleft palate traineeships should be sent to the Chairman, Committee on Traineeships and Fellowships, University of Pennsylvania, School of Dentistry, 4001 Spruce Street, Philadelphia 4, Pennsylvania. Inquiries for the traineeships in periodontology should be sent to: Dean, Graduate School of Medicine, 237 Medical Laboratories, University of Pennsylvania, Philadelphia 4, Pennsylvania.

NEW YORK UNIVERSITY COLLEGE OF DENTISTRY

The Periodontia and Oral Medicine Department will give a six-session course on the Temporomandibular Joint Dysfunction and its treatment by Dr. Sidney E. Riesner, Clinical Professor in the Department of Periodontia and Oral Medicine and Dr. Earl O. Butcher, Professor and Chairman of the Department of Anatomy. Monday, Wednesday, Friday, 9:30 A.M.-11:30 A.M. January 9th-January 20th, 1961.

The course will cover the anatomy and physiology of the joint. Pain symptoms, pathological disturbances, the role of dental occlusion, masticatory habits and psychogenic factors involved in the syndrome will be carefully analyzed. Methods of therapy by drugs and occlusal equilibration techniques will be examined. The utilization of stereoroentgenography for diagnosis will be demonstrated. Enrollment limit 10.

Tuition—$100.00. Please make checks payable to the College of Dentistry, Post Graduate Division, 421 First Avenue, New York 10, N. Y.

UNIVERSITY OF PITTSBURGH SCHOOL OF DENTISTRY

Applications are now being accepted by the Graduate Division of the University of Pittsburgh School of Dentistry for graduate study in the fields of Anesthesiology, Oral Surgery, Orthodontics, Periodontics, and Prosthodontics, leading to the Master of Science degree. Selection of students for the Fall Session of 1961 will be made in March, 1961.

A non-degree, full-time, twelve month course in General Anesthesia is also available for qualified dental graduates.

Graduate study in the pre-clinical basic sciences of Anatomy, Biochemistry, Microbiology, Pathology, Pharmacology and Physiology leading to the Master of Science or Doctor of Philosophy degrees is also offered through the Schools of the Health Professions. Successful applicants in this latter program are eligible for financial assistance in the form of traineeships.

For further information and application forms write to: Director of Graduate Education, University of Pittsburgh, School of Dentistry, Pittsburgh 13, Pa.

MICHAEL REESE HOSPITAL AND MEDICAL CENTER PRESENTS FOR THE THIRD CONSECUTIVE YEAR "THE MEDICAL LABORATORY IN CLINICAL DENTISTRY"

Thurs. Feb. 9 and Fri. Feb. 10, 1961 immediately following the Chicago Mid-winter Meeting.

Dr. Emanuel Cheraskin, Professor and Head of Department on Oral Medicine, University of Alabama, will present the nature of oral disease, the significance of laboratory findings, the physiology and pathology of blood and urine, tests for infectious diseases, chemical intoxication, neoplasia, stress syndrome, nutrition and hormonal deficiencies, hemorrhagic diathesis, as well as illustrate how they may be utilized in the practice of dentistry. Dr. Arthur Elfenbaum, Professor Emeritus, University of Illinois and Northwestern University, and in charge of Diagnostic division, Department of Dentistry, Michael Reese Hospital, will moderate the discussions.

As an innovation this year instead of the usual mimeographed manual, a printed textbook "Laboratory Aids in Stomatologic Diagnosis" by Dr. Cheraskin will be included with the course.

The fee for the two-day course will be $50.00.

For further information and the detailed program, write to Dental Department, Michael Reese Hospital, 29th Street and Ellis Ave., Chicago 16, Illinois.

THE WILLIAM J. GIES FOUNDATION FOR THE ADVANCEMENT OF DENTISTRY, INC.

At the banquet of the American Association of Dental Editors meeting in Los Angeles, California, Dr. Ascher L. Jacobs, D.D.S., today received the William J. Gies 1959 Editorial Award for his editorial entitled, "Dentistry and Apathy," which appeared in the Illinois Dental Journal in April, 1959.

Dr. Bissell B. Palmer, President of the William J. Gies Foundation for the Advancement of Dentistry, Inc., presented Dr. Jacobs with a silver plaque and a check for $200.00.

Dr. Jacobs is in general practice in Chicago, Illinois, and is an associate editor of the Illinois Dental Journal.

The William J. Gies Editorial Award is an annual event. Graduate dentists are invited to submit one or more editorials for the 1960 award, each limited to

750 words and published in non-proprietary dental journals in the United States or Canada during 1960, to the William J. Gies Foundation for the Advancement of Dentistry, Inc., 221 Park Avenue South, New York 3, New York, by March 1, 1961. Participants are requested, whenever possible, to send 3 copies of each editorial, identified with the name of the writer, publication name and date.

FEDERATION DENTAIRE INTERNATIONALE

The first annual meeting of the Federation Dentaire Internationale held in conjunction with the annual session of the American Dental Association was held in Los Angeles on Monday, October 17. The size of the meeting and the enthusiasm displayed relative to F.D.I. possibilities indicated a continually increasing group with the knowledge of the possibilities of the F.D.I.

Practically all organizations of every type have representation today at the international level. The F.D.I. during the past several years has been working with the World Health Organization (W.H.O.) and consequently dental Health programs are parallelling the W.H.O. health programs throughout the world.

Medicine has the two representatives at the international level, The World Health Organization and the World Medical Society. The dental profession has only the one international contact and that is through the Federation Dentaire Internationale. Certainly the prestige and the serviceability of dentistry dictates the positive necessity of having dentistry represented at the international level.

The 1961 annual meeting of the Federation will be held at Helsinki, Finland, July 9 to 16. The present interest manifest in the meeting indicates that there will be a large number of USA dentists who will attend the meeting. All those interested may contact Dr. Obed H. Moen, 6 Main Street, Watertown, Wisconsin, USA, National Treasurer for the FDI.

Application for Membership

FEDERATION DENTAIRE INTERNATIONALE

I wish to become a Supporting Member of the Federation Dentaire Internationale and subscribe to the International Dental Journal.

Name .....
(PLEASE PRINT)

Degrees .....

Address .....
(PLEASE PRINT)

I am a Member of the American Dental Association.

I enclose $15.00 for Supporting Membership and subscription to the International Dental Journal for the year .....

PLEASE COMPLETE AND RETURN WITH YOUR REMITTANCE TO

OBED H. MOEN

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S.S. HOPE

"The Djakarta dental association members came on board and immediately established rapport with me and my dental hygienist. They are friendly people and anxious to exchange information."

This is a report from an American dentist aboard the teaching and training ship HOPE, currently in Indonesia on a two-fold mission; to symbolize the genuine desire of Americans for peace and to help train native medical workers to be able to meet their own problems.

Stanley Hellman, D.D.S., of Chicago, wrote from the Indonesian island of Surabaya to Dr. William B. Walsh, president of Project HOPE:

"We have had several seminars both on board and at their school. The need for dentists is great; there are only 450 dentists for 86,000,000 people. Their three dental schools cannot produce enough dentists to keep up with the tremendous demand."

The HOPE, supported by contributions from Americans in all walks of life, has been received by the Indonesian press as representing "the heart of a mighty nation."

At the beginning of the new year, the HOPE will be farther and farther from the capital of Indonesia and it will travel among the outlying islands which make up this island country—Sumbawa, Makassar, Ambon, Kupang, Lombok and Semarang. In addition to teaching and training sessions on the ship, the Indonesian and American medical personnel aboard the vessel will divide up into teams and go into inland areas in an effort to reach as many native pupils as possible.

The need is great, both for monetary contributions and for dental volunteers to serve aboard the vessel. Information can be secured directly from Henry A. Swanson, D.D.S., National Dental Chairman, Project HOPE, 1818 M Street, N. W., Washington 6, D. C.

THE AMERICAN SOCIETY OF PSYCHOSOMATIC DENTISTRY AND MEDICINE

The annual meeting of the American Society of Psychosomatic Dentistry and Medicine will be held at the Shoreham Hotel, Washington, D.C., beginning Friday evening, March 10th, to Sunday afternoon, March 12th, 1961 immediately preceding the District of Columbia Dental Society meeting. The main theme of the program will be *Anxiety*, Its Recognition and Handling in the Clinical Setting of General Practice. On Saturday and Sunday morning round table discussions will be held in the utilization of hypnosis in the various specialties of general practice. All dentists and physicians are cordially invited to attend. For the detailed program, contact Dr. Jesse Caden, Chairman, Program Committee, 5213 Connecticut Avenue, N.W., Washington 15, D.C.

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